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WALTER WYMAN, Surgeon-General.

HYGIENIC LABORATORY.—BULLETIN No. 23.

AUGUST 1, 1905.

CHANGES IN
THE PHARMACOPŒIA OF THE
UNITED STATES OF
AMERICA

EIGHTH DECENNIAL REVISION.

(Official from September 1, 1905.)

By

REID HUNT

and

MURRAY GALT MOTTER.



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ABBREVIATIONS.

Br. P.....	British Pharmacopœia, 1898.
P. G.....	Pharmacopœa Germanica IV.
T. S.....	U. S. P. Test Solution.
N. F.....	National Formulary (1896).

CHANGES

IN THE

PHARMACOPŒIA OF THE UNITED STATES OF AMERICA, EIGHTH DECENNIAL REVISION.

(Official from September 1, 1905.)

By REID HUNT, M. D.,

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INTRODUCTION.^a

ORIGIN AND SCOPE OF BULLETIN.

The United States Pharmacopœia is the official standard for the U. S. Public Health and Marine-Hospital Service. Drugs purchased for its hospitals and relief stations must conform to the Pharmacopœial requirements. A circular letter, calling the attention of the medical officers and pharmacists of the Service to the many and important changes in the revised edition, was at first contemplated. It was believed that such a letter would aid these officials in their study of the revised Pharmacopœia and facilitate the early adoption of the new names and new preparations. Later, with the approval of the Board of Trustees of the Pharmacopœial Convention, it was decided to publish this information in the form of a bulletin. It is believed that such a bulletin will help the practitioner to a better understanding of the significance of some of the innovations. Being written for physicians, only such changes are discussed in this bulletin as are of interest and use to them, such, for example, as changes in the strength of preparations, changes in name, the additions, etc. For changes relating to methods of preparation, of tests for identity, purity, etc., the reader is referred to the Pharmacopœia itself.

^a The authors are greatly indebted to Dr. Daniel Base, of the Division of Pharmacology, for valuable assistance rendered in the preparation of this bulletin.

Special attention is directed to the following points:

1. *Terminology*.—The general plan regarding terminology is expressed in the following extract from the General Principles to be Followed in Revising the Pharmacopœia, adopted by the Pharmacopœial Convention of 1900:

“* * * In the case of newly admitted articles it is recommended that such titles be chosen as are in harmony with general usage and convenient for prescribing; but in the case of chemicals of a definite composition a scientific name should be given, at least as a synonym.”

In accordance with this general principle a large number of synthetic remedies have been admitted into the Pharmacopœia, not under their trade or commercial names by which many are well known to the profession, but, in most cases, under names approximating, as closely as practicable, their true chemical names. Thus “Phenacetin” is admitted as *Acetphenetidinum*, a name which shows at once that this substance belongs to the great group of phenetidin compounds. “Aristol” is admitted as *Thymolis Iodidum*, a name showing that this substance is an iodine compound of thymol. While a few of these new names may at first lead to some confusion, it is certain that they will ultimately greatly simplify not only the terminology, but also our understanding of the nature and use of such substances. For example, at present the same chemical compound is sometimes put on the market under a variety of commercial names. Thus, hexamethylene tetramine is sold under at least seven different names, most of which refer in a vague way to some supposed therapeutic value of the drug, and not to its chemical nature. The Pharmacopœia admits this substance under the name *Hexamethylenamina* and fixes a standard of purity. By demanding the U. S. Pharmacopœia article the physician is not only assured a product of uniform high quality, but he aids in reducing the multiplicity of names which is so often a source of confusion. Because of the different names under which a given drug is sold, it is no wonder that physicians who have failed to secure the results expected from a certain drug have prescribed it again under a different name, but with the impression that they were trying something new.

The use of the chemical names, as far as practicable, is also a great aid in classifying the compounds which are being put upon the market in such ever increasing numbers. If the physician understands the chemical nature of a comparatively few well-known substances he will more readily see the relations of the new ones to these, and will appreciate how slight many of the modifications are. In fact, notwithstanding the number of the latter, drugs of distinctly new therapeutic properties are rare.

Aside from the evident desirability of having names at least suggesting the chemical nature of the drug, there is another reason for giving preference to the Pharmacopœial names. A substance is often

sold under a fanciful, registered name at a much higher price than under the chemical name. Thus a hardship is worked on pharmacist and patient alike.^a

The general principle of using, whenever practicable, the true chemical name of a substance has been extended to a number of drugs which were already official in the U. S. Pharmacopœia. Thus, Acidum Carbolicum (U. S. P., 1890) (a name no longer approved in chemical terminology), becomes *Phenol*; the composition of Salol (U. S. P., 1890) is shown by its new official name, *Phenylis Salicylas*, etc.

The "Extracta Fluida" becomes *Fluidextracta*; thus these preparations are separated alphabetically from the other extracts, and much confusion is thereby obviated.

2. *Changes in strength*.—A number of very important changes have been made in the strength of certain preparations. "The International Conference for the Unification of the Formulas of Heroic Medicines," held at Brussels in 1902, recommended that certain preparations of the heroic remedies be made of uniform strength in the pharmacopœias of the different countries. The present revision of the U. S. Pharmacopœia has accepted nearly all of the recommendations adopted by this conference. The tincture of aconite, for example, is reduced from 35 per cent to 10 per cent, the tincture of cantharides is increased from 5 per cent to 10 per cent, etc. The great majority of tinctures are now of either 10 or 20 per cent strength; the most noteworthy of those of the 10 per cent class, besides aconite and cantharides, just mentioned, are those of digitalis, squill, and strophanthus. These changes have been classified and tabulated for this bulletin.

The increase in the scope of pharmacopœias is an interesting chapter in the history of medicine. Before the publication of the first U. S. Pharmacopœia (in 1820) various European pharmacopœias were the chief standards for this country, although the United States Army, the Massachusetts Medical Society, and the New York Hospital had previously issued pharmacopœias of more than local importance. It was not until 1864 that there was a national British Pharmacopœia; prior to that year three pharmacopœias were in use in Great Britain—the London, the Edinburgh, and the Dublin. The U. S. Pharmacopœia, in adopting the suggestions of the Brussels Conference, is the first pharmacopœia to acquire an international scope.^b

^aTo obviate this unnecessary increase of expense to the patient a Government order was recently issued in Germany directing the official physicians to the poor to prescribe drugs under their Pharmacopœial instead of under their registered names.

^bThe growing tendency to give wider recognition to official standards is well shown by the fact that, in several States, drugs not in the U. S. Pharmacopœia are deemed adulterated if they do not conform to the standards of purity of foreign pharmacopœias.

3. *Additions*.—There are 117 additions in the Eighth Decennial Revision of the U. S. Pharmacopœia; among these are representatives of all classes of drugs. There is, for instance, a larger number of synthetic remedies than ever before. The principles involved in the pharmacopœial terminology of these have already been discussed. The active principles of a number of drugs have been admitted; this permits of more accurate dosage and their use obviates the necessity of administering inert and often undesirable constituents of the crude drug. New salts of well-known drugs have been admitted on account of their greater stability or solubility. Inasmuch as the discovery of diphtheria antitoxin is perhaps the greatest achievement in therapeutics in the last quarter of a century, the *Serum Antidiphthericum* is a very notable addition to the Pharmacopœia; not only is this substance made official but a definite American standard for it has been fixed.

A class of additions deserving careful consideration by the medical profession is represented by certain of those combinations of well-known drugs which in recent years have become popular with physicians and also with the laity. Some of these preparations are extensively sold under various trade names, and the manufacturers have not always made public their constituents; the same name is sometimes applied by different manufacturers to different combinations. Recognizing the demand for such preparations a number of them have been admitted into the Pharmacopœia, and the proportions of the ingredients fixed, thereby giving physicians the opportunity of securing uniform preparations, the constituents of which are of known strength and purity.

The introduction of these various preparations reduces to a very small number those extra-pharmacopœial drugs which the conservative, well-informed physician will desire to prescribe. There are undoubtedly a few drugs not in the Pharmacopœia which many physicians have found to be of distinct value; most of these are protected by patents and could not be admitted under the rules formulated by the Pharmacopœial Convention. The pharmacopœial preparations, however, will in most cases meet the needs of physicians who are accustomed to consider carefully the chemical nature and the physiological action of a drug before they venture to use it, and who know how rarely a distinctly new drug with real advantages over those already in use is discovered.

4. *Assay processes*.—A noteworthy feature of the revised Pharmacopœia, and one which places it at the head of the pharmacopœias of the world in this respect, is the introduction of a large number of assay processes for important drugs of vegetable origin. An examination of the tables given in this bulletin (pp. 65–66) will show that standards of strength and methods for confirming them have been

introduced for over fifty important official preparations for which no such requirements were made in the 1890 Pharmacopœia.

Before the introduction of assay methods the pharmacist and physician were compelled to judge the quality of drugs largely by their appearance; from this it was possible to determine in many cases whether medicinal plants, for example, had been collected and cared for in a way which would *probably* preserve their therapeutic virtues. In many cases, however, the physician was compelled to rely solely upon the therapeutic test. Great credit is due those manufacturers who for years have been perfecting processes of assay and placing upon the market preparations of definite strength of many of the most important drugs.

The introduction into the Pharmacopœia of such a large number of these assay processes will now insure a more general uniformity in the purity, strength, and therapeutic action of pharmacopœial preparations than ever before, and the entire medical profession is under lasting obligations to the Committee of Revision who have labored so long to perfect as nearly as possible these assay methods. Unfortunately there still remain a number of pharmacopœial preparations for which no definite method of chemical analysis or assay has been devised. Among these may be mentioned the *Serum Antidiphthericum*, already referred to. Another group embraces certain galenicals, the active principles of which are as yet either not sufficiently known or are incapable of isolation and assay by present methods. Although care in the selection and in the manufacture of the materials will in many cases insure preparations of therapeutic value, yet, for the careful standardization of such, recourse is had to physiological methods; but physiological methods of standardization were specifically barred from the Pharmacopœia by the Pharmacopœial Convention of 1900. The reasons for this are obvious; assay processes introduced into the Pharmacopœia are such as every well-equipped pharmacist is able to apply. It is not to be expected, however, that even the best-equipped pharmacist should have the theoretical knowledge, the technical training, and the material facilities for biological and physiological investigations. Recognizing the increasing demand for standardized preparations, certain manufacturing establishments have been equipped not only with pharmaceutical and chemical laboratories of the most approved type, but with biological laboratories as well, the work and products of which are a credit alike to commercial enterprise and to genuine scientific progress.

5. *Purity rubric*.—Whenever practicable a minimum degree of purity has been fixed and requirements established which exclude objectionable impurities.

6. *Doses*.—The Pharmacopœial Convention instructed the Committee of Revision “to state the average approximate (but neither a

minimum nor a maximum) dose for adults," and further directed it to declare "that neither this Convention, nor the Committee of Revision created by it, intends to have these doses regarded as obligatory on the physician or as forbidding him to exceed them whenever in his judgment this seems advisable." A table of these doses has been compiled and inserted in this bulletin.

RELATION OF PHYSICIANS TO THE PHARMACOPŒIA.

A few words may be added regarding the relation of the physician to the Pharmacopœia. The U. S. Pharmacopœia had its origin in the medical profession, and the early editions were entirely the work of physicians. Although so vitally interested in the Pharmacopœia—for in many cases it is the physician's sole legal guarantee of the quality of the drugs he uses—and although medical men are always represented on the Committee of Revision, the medical profession as a whole can scarcely be said to give the publication the support it deserves: physicians often prescribe proprietary drugs or articles under commercial names when a greater familiarity with the Pharmacopœia would show that there are official preparations of similar character but of more uniform composition. The authority of the Pharmacopœia, however, is steadily increasing: nearly half the States have made it the legal standard for drugs, and whenever a "pure drug bill" is proposed it is assumed, almost as a matter of course, that the U. S. Pharmacopœia is to be the standard by which the quality of drugs is to be judged. Despite the fact that there may, and of necessity always will, be certain minor imperfections in the Pharmacopœia, it is and will remain the leading standard; and no one questions the imperative need of such a standard.

The need of such a standard for drugs intended for the use of physicians is all the more evident when it is remembered that some manufacturers who do make standard pharmacopœial preparations nevertheless frankly admit that they put upon the market other preparations of the same substance by no means of pharmacopœial standard but under names almost identical with the pharmacopœial names. These manufacturers claim that, when the official article is not specifically designated, popular demand and commercial competition justify this procedure. The possible dangers in such a course must at once be apparent, and this practice is one of the reasons for the legal requirement in many States that any article sold under a pharmacopœial name must conform to pharmacopœial standards.

The Pharmacopœia is moreover the chief bulwark of one of the most time-honored principles of the medical profession, namely, that there must be no secrets about the drugs used in the treatment of disease. Upon this question, that physicians must have full knowledge of all the constituents and of all the properties of the drugs they prescribe,

there can be no compromise. The physician should never forget that he is the sole judge of what is suitable for his patient.^a

Not only does the individual patient often suffer, but real progress in therapeutics is delayed by the use of remedies as to the composition of which the physician has but imperfectly informed himself; in many cases were the real nature of the drug made known the physician would see the folly of using it. The mythical character of the virtues claimed for some "special combinations" has been repeatedly shown by chemical analysis.^b Thus some of the remedies advertised to physicians under fanciful names, with very vague descriptions of their composition but with full directions for use, have been shown to be nothing but mixtures of some of the best-known U. S. Pharmacopœia drugs.

The Pharmacopœia is often criticised for retaining and admitting drugs which many physicians regard as useless. It should be remembered, however, that the Pharmacopœia is (and under our form of government must be) representative, as well as conservative; the framers endeavor to make it reflect the actual demands of the medical profession.^c

^a That the assurances as to the virtues of secret or semi-secret preparations, although made in good faith and supported by high authority, are not a sufficient safeguard against dangerous accidents, is illustrated by the following case: Some manufacturers who prepared certain tinctures with methyl alcohol attempted to justify their departure from recognized pharmaceutical methods by claiming that methyl alcohol is a better solvent of some of the constituents of ginger than is ethyl alcohol, and this claim, as well as the contention that methyl alcohol is not more toxic than ethyl alcohol, was supported in court by the testimony of high official chemists; the plaintiff in the case in question (a physician whose sight was destroyed by the methyl alcohol) thought when he bought this preparation that he was buying an article made according to the Pharmacopœia.

^b See, for example, the reports of the Council on Pharmacy and Chemistry of the American Medical Association.

^c The scope of the Pharmacopœia is well described in the following words of H. C. Wood, President of the U. S. Pharmacopœial Convention (Pop. Sci. Monthly, Jan., 1905, p. 279):

"A common, fallacious belief is that Pharmacopœial recognition means that the drug recognized is of value; the fact is that the United States and other Pharmacopœias have in them numerous drugs of very little use. The nature or *motif*, so to speak, of a Pharmacopœia is not to distinguish between worthy and worthless drugs, but to see that a drug which is asked for is, as sold by the apothecary, pure, and that proper preparations of uniform strength are made by the apothecary.

"The question which the framers of a Pharmacopœia ask themselves is not, Is this drug of value, but Is there a demand for it by the profession of medicine? If five thousand doctors in the United States believed brick dust to be a valuable remedy and habitually used it, brick dust would have to go into the Pharmacopœia. Witch-hazel is probably as active and as useful as is brick dust, but witch-hazel is a fad and is enormously called for, and so witch-hazel must go into the Pharmacopœia. The Pharmacopœia exists for the purpose of requiring the apothecary to give, in the first place, pure brick dust or pure witch-hazel when asked for; and, in the second place, uniform preparations of these remedies."

If obsolete drugs are retained or new ones of proved value fail to gain admission to the Pharmacopœia it is because the medical profession of the country fails, through lack of concerted action (as by means of the national or local medical societies) to make their wishes sufficiently clear.^a

No account of the Eighth Decennial Revision of the Pharmacopœia would be complete without an expression of the gratitude which all physicians must feel to the Committee of Revision who, with no motives other than their interest in higher standards, have labored so long and well to perfect as nearly as may be the U. S. Pharmacopœia.

^a When the Pharmacopœial Convention of 1900 met, only five medical organizations presented recommendations and suggestions for the revision of the Pharmacopœia.

ADDITIONS TO THE PHARMACOPŒIA.

ACETONUM.

Acetone.



“A liquid containing not less than 99 per cent by weight of absolute acetone.” (U. S. P.)

Chemically, acetone is dimethyl-ketone (CH_3COCH_3). It is present to a considerable extent in crude wood alcohol.

Properties.—Clear, colorless, mobile, neutral liquid, inflammable, and having an ethereal odor and taste. Specific gravity, 0.790 (25° C.); boiling point, 56.5° C. Miscible with water and alcohol in all proportions. An excellent solvent for fats, resins, rubber, etc. Iodoform is formed when acetone is slightly warmed with an alkali and iodine (basis of method for determining acetone in diabetic urine, etc.); it also yields iodoform with an alcoholic solution of iodine and ammonia (Gunning’s test; difference from alcohol). Acetone forms with nitroprussiate of soda and sodium hydroxide a reddish-brown color, which passes into purple or violet on acidifying with acetic acid (Legal’s test).

Use.—Acetone is used extensively in the manufacture of chloroform, iodoform, and sulphonmethane (q. v.). A number of oleoresins (aspidium, capsicum, ginger, lupulin, and pepper) formerly prepared (U. S. P., 1890) with ether are now prepared with acetone, as the latter is neither so inflammable nor so expensive as the former.

Acetone seems to be slightly more poisonous than ethyl alcohol; the symptoms caused by the two are, generally speaking, similar.

Caution.—It should be kept in well-stoppered bottles remote from lights or fire.

Related Compounds.—When a phenyl radical (C_6H_5) takes the place of one of the methyl groups in acetone, the resulting compound is phenyl-methyl-ketone ($\text{C}_6\text{H}_5\text{COCH}_3$), also known as acetophenone. This has been used as a hypnotic under the name of *Hypnone*. It is a liquid above 20.5° C. *Malarine* is a condensation product of acetophenone and paraphenetidin (see Acetphenetidin). It is usually employed in the form of the citrate.

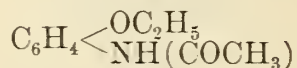
Salacetolum is a salicylic acid ester of acetol which is an alcohol ($\text{CH}_3\text{COCH}_2\text{OH}$) derived from acetone; proposed as an antirheumatic.

Acetoacetic acid, also called diacetic acid ($\text{CH}_3\text{COCH}_2\text{COOH}$), which may be looked upon as acetone in which a hydrogen atom has been replaced by the acid group (COOH), is found in the urine in many cases of diabetes mellitus. It is thought that one source of acetone found in diabetic urine is the decomposition of diacetic acid.

ACETPHENETIDINUM.

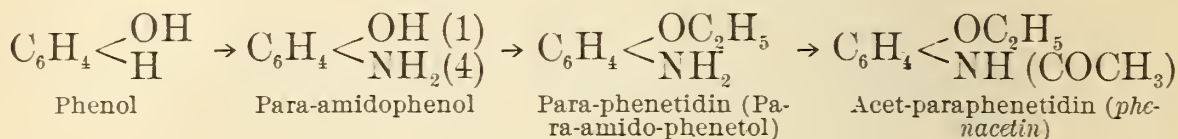
Acetphenetidin.

(*Phenacetin.*)



This substance is generally known by the trade name *phenacetin*; official in the British, German, and Swiss Pharmacopœias as Phenacetinum; also called para-acetphenetidin.

Chemistry.—The derivation of acetphenetidin is shown by the following formulas:



It may be regarded as acetanilide ($\text{C}_6\text{H}_4 < \begin{smallmatrix} \text{H} \\ \text{NH}(\text{COCH}_3) \end{smallmatrix}$) in which one hydrogen atom is replaced by the ethoxy group (OC_2H_5).

Character.—“White, glistening, crystalline scales, or fine crystalline powder, odorless, and tasteless.”

Solubility.—Slightly soluble in water (1:925), much more so in boiling water (1:70), and still more in alcohol (1:12).

Purity.—Occasionally adulterated with acetanilide, which may be recognized by the following Pharmacopœial test:

“If 0.1 Gm. of Acetphenetidin be boiled with 10 Cc. of water it should yield a solution which, when cooled and filtered, should not become turbid upon the addition of bromine T. S. [1 per cent solution] in slight excess (absence of acetanilide).”

For other tests, see the Pharmacopœia and Kebler, Lyman F.: *Adulterated drugs and chemicals*, U. S. Dept. Agric., Bur. Chemistry, Bull. No. 80, 1904.

Incompatibility.—Incompatible with phenol, chloral hydrate, iodine, salicylic acid, and oxidizing agents.

Dose.—“Average dose: 0.500 Gm. = 500 milligrammes ($7\frac{1}{2}$ grains).” (U. S. P.)

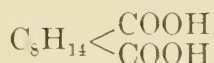
Caution.—The German Pharmacopœia states that not more than 3 Gm. (45 grains) should be given in the course of a day. Special caution should be observed when acetphenetidin is prescribed in combination with other drugs of similar physiological action; thus, acetanilide and acetphenetidin should not be combined in full dose of each.

Excreted in the urine as amidophenol or amidophenetol, which gives a red color with ferric chloride; also causes appearance of a reducing substance.

Similar Compounds.—This is the representative of a very large number of similar compounds known as the phenetidin series. These are derived from para-amidophenol $\left(\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OH} \\ \text{NH}_2 \end{smallmatrix} \right)$ by replacing the hydrogen atom of the hydroxyl group and one or both of the hydrogen atoms of the amido (NH_2) group by alkyl or acid radicals. Thus, *lactophenin* is formed when the lactyl group ($\text{COCH}(\text{OH})\text{CH}_3$) is introduced into para-phenetidin instead of the acetyl (CH_3CO) group: $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OC}_2\text{H}_5 \\ \text{NHC} \end{smallmatrix} \text{COCH}(\text{OH})\text{CH}_3$. *Sedatin*,^a *apolysin*, *citrophen*, *kryofin*, *malakin*, *salophen*, *saliphen*, *phenocoll*, *salocoll*, etc., are similar compounds. The physiological action of all these substances is fundamentally the same. These compounds, as well as acetphenetidin itself, are contained in many migraine and headache powders. *Chinophenin* and *eupyrine* are also phenetidin compounds.

ACIDUM CAMPHORICUM.

Camphoric Acid.



“A dibasic organic acid obtained by the oxidation of camphor.” Official under same name in the German Pharmacopœia.

Of the various camphoric acids known, only the dextro-rotatory is official. It is prepared by oxidizing camphor with nitric acid.

Character.—Colorless, odorless crystalline plates, or a crystalline powder having an acid, bitter taste. Melting point, 187°C . It forms easily soluble salts with the alkalies.

Solubility.—Difficultly soluble in cold water (1:125), more readily in boiling water (1:10); readily soluble in alcohol; soluble in fatty oils (1:50).

Purity.—Should not have the odor of camphor; tested by the U. S. Pharmacopœia method should be free from nitric acid.

Action.—The general symptoms produced by camphoric acid are similar to those caused by camphor, but the latter is much more powerful. Used as an antihydrotic in doses of 1 to 2 Gm. and (in solution) as a local astringent in the nose, throat, and bladder. As it is but slightly soluble in water, it has been recommended in making solutions to add 11 per cent of alcohol for each per cent of camphoric acid.

Dose.—“Average dose: 1 Gm. (15 grains).” (U. S. P.)

Guakamphol is a combination of Guaiacol and Camphoric Acid.

^a The name *sedatin* has also been used as a synonym for antipyrine.

ACIDUM HYDRIODICUM DILUTUM.

Diluted Hydriodic Acid.

HI

"A solution of hydriodic acid containing not less than 10 per cent by weight of the absolute acid, and about 90 per cent of water."

This is a reintroduction, the preparation having been admitted to the U. S. Pharmacopœia of 1860, but dismissed on account of the difficulty of preserving it.

In the present preparation there is a small quantity of hypophosphorous acid. This acts as a preservative by reducing any iodine set free to hydriodic acid. The method of preparing it (for which see the Pharmacopœia) is that recommended in the 1890 U. S. Pharmacopœia in connection with the preparation of Syrupus Acidi Hydriodici; the latter is now prepared from the Acidum Hydriodicum Dilutum. The method is simple and requires no special apparatus or chemicals.

Character.—A clear, colorless liquid, odorless and having an acid taste. It should not become colored on keeping. Miscible in all proportions with water or alcohol.

Dose.—"Average dose: 0.5 Cc. (8 minims)." (U. S. P.)

Caution.—"Should be kept in small, amber-colored, glass-stoppered bottles, protected from the light."

ACIDUM HYPOPHOSPHOROSUM.

Hypophosphorous Acid.

 $\text{H}_2\text{P}_2\text{O}_5$

"A liquid composed of 30 per cent by weight of absolute hypophosphorous acid and 70 per cent of water."

Properties.—A colorless, odorless liquid having an acid taste. Miscible in all proportions with water. It is a powerful reducing agent, precipitating metallic silver from solutions of silver nitrate, calomel from corrosive sublimate, etc.: when heated with copper sulphate a yellow precipitate of copper hydride is formed (difference from phosphorous acid).

It is used in the preparation of Acidum Hypophosphorosum Dilutum.

Incompatibilities.—Incompatible with arsenical salts, and in general with substances that are more or less easily reduced.

ACIDUM TRICHLORACETICUM.

Trichloroacetic Acid.

 CCl_3COOH

"A monobasic organic acid usually obtained by the oxidation of hydrated chloral with nitric acid."

Properties.—White, deliquescent, rhombohedral crystals, having a slight, characteristic, mildly pungent odor.

Very soluble in water and alcohol; in the latter, part of the acid is changed into the ester.

The aqueous solution on boiling is decomposed with the formation of chloroform and carbon dioxide: $\text{CCl}_3\text{COOH} = \text{CHCl}_3 + \text{CO}_2$.

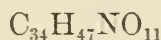
Ten parts of trichloroacetic acid and 1 part of water form a liquid known as acidum trichloroaceticum liquefactum; it is often dispensed in this form (cf. Phenol Liquefactum).

It precipitates proteids and is used as a reagent for the detection of albumin in urine and milk.

Caution.—"Should be kept in dark, amber-colored, well-stoppered bottles in a cool place." It is far stronger than acetic acid and should be used with great caution.

ACONITINA.

Aconitine.



An alkaloid obtained from Aconite. Official in the Br. P.

The chemical structure of aconitine is analogous to that of atropine and cocaine; like the latter it undergoes partial decomposition when boiled for some time with water.

Properties.—Colorless or white rhombic tables or prisms, odorless, permanent in the air, and producing in extremely diluted solutions a characteristic tingling sensation when brought in contact with the mucous membrane of the tongue or lips. The alkaloid itself should never be tasted, and its solution only when largely diluted, and then with the utmost caution.

Very slightly soluble in water (1:3200), much more so in alcohol (1:22).

Aconitine was formerly in the U. S. Pharmacopœia, but was dropped in 1880 owing to the variable composition of the article then on the market. At present there are on the market, in addition to the crystalline aconitine, an amorphous aconitine and an eclectic "aconitin." The greatest caution should be observed not to confuse these preparations, as they differ considerably in composition.

Aconitine is the most powerful drug in the Pharmacopœia; death is reported to have resulted from 0.5 milligramme ($\frac{1}{200}$ grain).

Dose.—"Average dose: 0.00015 Gm. = 0.15 milligramme ($\frac{1}{4000}$ grain)." (U. S. P.)

Aconitine is contained in the Oleatum Aconitinæ of the National Formulary.

ADEPS LANÆ.

Wool-Fat.

Adeps Lanæ, Br. P.; Adeps Lanæ anhydricus, P. G. "The purified fat of the wool of sheep, freed from water." The Hydrous Wool-Fat, which contains "not more than 30 per cent of water," is still

retained in the Pharmacopœia; if this be heated on the water bath, with stirring, until it ceases to lose weight, it is converted into Adeps Lanæ.

In making certain ointments, the water contained in hydrous wool-fat is objectionable; for such preparations Adeps Lanæ is preferable.

ÆTHYLIS CARBAMAS.

Ethyl Carbamate.

(Urethane.)



Ethyl Carbamate is defined as: "An ester of carbamic acid obtained by the reaction of ethyl alcohol upon urea (carbamide) or one of its salts." Reaction: $\text{CO} < \begin{smallmatrix} \text{NH}_2 \\ \text{NH}_2 \end{smallmatrix} + \text{HOC}_2\text{H}_5 = \text{CO} < \begin{smallmatrix} \text{NH}_2 \\ \text{OC}_2\text{H}_5 \end{smallmatrix} + \text{NH}_3$

Character.—"Colorless, columnar crystals or scales, odorless, and having a cooling saline taste."

Solubility.—Soluble in less than one part of water, and in 0.6 part of alcohol.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

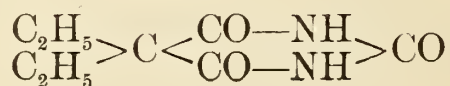
Larger doses do not as a rule increase the hypnotic effect, as the (NH_2) group stimulates the central nervous system in somewhat the way that ammonia (NH_3) does. Both Ethyl Carbamate (*urethane*) and *hedonal* (see below) frequently fail to produce sleep, probably owing to the stimulating action of the (NH_2) group.

Caution.—Should be kept in well-stoppered bottles.

This substance, generally known simply as *urethane*, is a member of a series of compounds called urethanes. They are esters of carbamic acid $\text{CO} < \begin{smallmatrix} \text{NH}_2 \\ \text{OH} \end{smallmatrix}$ which in turn is derived from carbonic acid

$\text{CO} < \begin{smallmatrix} \text{OH} \\ \text{OH} \end{smallmatrix}$ by the substitution of the amido group (NH_2) for one hydroxyl group (OH). Carbamic acid is not known in the free state, but only in the form of its salts. The ammonium salt is a constituent of the Pharmacopœial Ammonium Carbonate.

Related Products.—Closely allied to ethyl carbamate are: *hedonal* (methylpropylcarbinolurethane = $\text{CO} < \begin{smallmatrix} \text{NH}_2 \\ \text{O}-\text{CH} < \begin{smallmatrix} \text{CH}_3 \\ \text{C}_3\text{H}_7 \end{smallmatrix} \end{smallmatrix}$), *euphorine* or *phenylurethane* ($\text{CO}(\text{NHC}_6\text{H}_5)\text{OC}_2\text{H}_5$), *neurodin*, *thermodin* (*phenacetin-urethane*), etc. One of the latest additions to this group is the *veronal* of Emil Fischer and von Mering; this is diethylmalonylurea;



ÆTHYLIS CHLORIDUM.**Ethyl Chloride.**

Ethyl Chloride is “a haloid derivative, prepared by the action of hydrochloric acid gas upon absolute ethyl alcohol.” Also known as *chelene* or *kelene*.

Character.—“Colorless, mobile, very volatile liquid, having a characteristic, rather agreeable odor and a burning taste.” It boils at a temperature of 12.5° to 13° C.

Solubility.—Slightly soluble in water, readily in alcohol.

Purity.—“If 10 Cc. of ethyl chloride, while cold, be dissolved in alcohol, and a few drops of silver nitrate T. S. $\left[\frac{\text{N}}{10} \text{AgNO}_3\right]$ be added, no turbidity should be produced (absence of hydrochloric acid).”

Although ethyl chloride is usually used as a local anæsthetic, it is contained in the following mixtures intended for general anæsthesia:

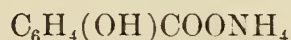
<i>Anæsthol</i>	{ Ethyl chloride 17 parts	} by weight.
	{ Chloroform 36 parts	
	{ Ether 48 parts	
<i>Somnoform</i>	{ Ethyl chloride 60 parts	} by weight.
	{ Methyl chloride 35 parts	
	{ Ethyl bromide 5 parts	

(Jour. Amer. Med. Assoc., April 22, 1905, p. 1303.)

“*Anæsthol* (Speier)” is a mixture of ethyl chloride and methyl chloride for local anæsthesia. *Anestyl* and *coryl* are also mixtures of ethyl chloride and methyl chloride.

Caution.—Very inflammable; should not be used in proximity to a gas flame or fire. It should be preserved in hermetically sealed glass tubes in a cool place.

As a permanent opacity may result when freezing mixtures come in contact with the cornea, Merz-Weigandt (Hirschberg's Festschrift, 1905, p. 187) emphasizes the necessity of caution when using ethyl chloride about the head.

AMMONII SALICYLAS.**Ammonium Salicylate.**

Character.—“Colorless, lustrous, monoclinic prisms or plates, or a white crystalline powder, odorless, and having at first a slightly saline, bitter taste, with a sweetish aftertaste. Permanent in dry air.” The concentrated aqueous solution reddens blue litmus.

Solubility.—Very soluble in water (0.9 part), slightly less so in alcohol (2.3 parts).

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

"Should be kept in well stoppered bottles, protected from heat and light."

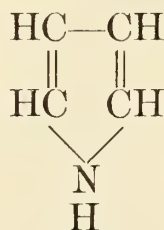
ANTIPYRINA.

Antipyrine.



Official in the Austrian and Swiss Pharmacopœias as Antipyrinum; now official in the German Pharmacopœia as Pyrazolonum phenyldimethylicum (formerly as Antipyrinum); in the British as Phenazonum, and in the French as Analgésine. Other names that have been applied to it are *anodynin*, *metozin*, *oxydimethylchinizin*, *parodyn*, *phenazon*, *phenylon*, *pyrazolin*, *sedatin*.

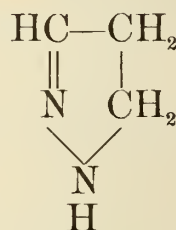
Chemistry.—Chemically it is phenyldimethylisopyrazolon; its derivation may be seen from the following formulas:



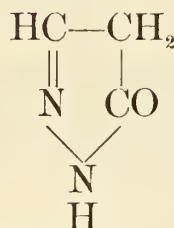
Pyrrol



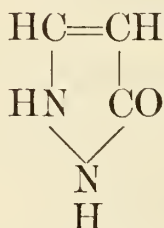
Pyrazol



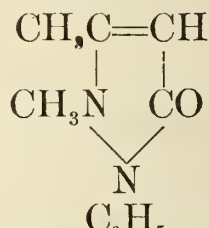
Pyrazolin



Pyrazolon



Iso-pyrazolon



Dimethyl-phenyl-
iso-pyrazolon

It is not obtained directly from the mother substance isopyrazolon, but is built up synthetically by condensation of phenylhydrazine with acetoacetic ether, and methylation of the product.

Character.—"A colorless, almost odorless, crystalline powder, or tabular crystals, with a slightly bitter taste."

Solubility.—Soluble in less than 1 part of water, and in 1 part of alcohol.

Purity.—"Two Cc. of an aqueous solution of Antipyrine (1 in 100) mixed with an equal volume of nitric acid assumes a yellowish color, passing to crimson on warming (distinction from acetanilide and acetphenetidin)."

"On warming 0.1 Gm. of Antipyrine with sodium hydroxide T. S. [Liq. Sodii Hydroxidi] and again warming after the addition of chloroform, the disagreeable odor of phenyl-isocyanide should not be developed (absence of acetanilide)."

Incompatibilities.—Hager's Handbuch der pharmaceutischen Praxis calls attention to the incompatibility of Antipyrine with a large number of substances and the production therewith of unexpected changes; among these may be mentioned:

(1) Antipyrine and nitrous acid, or substances which can evolve nitrous acid, as, for instance, Amylis Nitris and Spiritus Ætheris Nitrosi; a green color results from the formation iso-nitroso-antipyrine.

(2) Antipyrine and Mercurous Chloride (calomel); a very poisonous organic mercury compound is formed in a mixture of these substances.

(3) Antipyrine and Phenol, even in dilute aqueous solution, form an oily mass.

(4) Antipyrine and Sodii Salicylas, when rubbed together in powder, form a pasty mass; in solution they do not seem to affect each other.

(5) Antipyrine and Betanaphthol give a moist mixture.

(6) Antipyrine and Hydrated Chloral, rubbed together, form an oil which no longer gives the reactions of the components.

(7) Tannic acid precipitates Antipyrine as a tannate.

On the other hand, Antipyrine increases the solubility in water of caffeine and the quinine salts.

Allied Compounds.—Antipyrine unites with resorcin to form *resopyrin*, with salicylic acid to form *salipyrin*, with chloral hydrate to form *hypnal* and other compounds. *Pyramidon* is a dimethylamido substitution product of antipyrine. *Ferripyridin* is a combination of ferric chloride and antipyrine. Many other compounds are known. Antipyrine is a constituent of many "migraine powders."

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

Caution.—On account of the wide range of incompatibilities already indicated, the greatest caution should be observed in combining antipyrine with other substances.

AQUE.

Waters.

Medicated Waters.

"The Medicated Waters, when prepared from volatile oils, are intended to be, as nearly as practicable, saturated solutions, which must be clear, and free from solid impurities."

This is a new title under which various methods of preparing official waters of volatile oils are briefly outlined. In the method especially recommended by the Pharmacopœia, in a number of cases, the solution of the volatile oils is facilitated by the use of purified talc, instead of by precipitated calcium phosphate, as in U. S. Pharmacopœia, 1890.

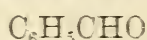
AQUA HAMAMELIDIS.**Hamamelis Water.**

The final product here is a distillate, while the old *Extractum Hamamelidis Fluidum* is a percolate now designated *Fluidextractum Hamamelidis Foliorum*.

The aqua contains about 15 per cent of alcohol.

Dose.—"Average dose: 8 Cc. (2 fluidrachms)." (U. S. P.)

This preparation is almost identical with *Aqua Hamamelidis Spirituosa*, N. F.

BENZALDEHYDUM.**Benzaldehyde.**

"Produced artificially or obtained from natural oil of bitter almond or other oils, and containing not less than 85 per cent of pure benzaldehyde."

Properties.—"Colorless, strongly refractive liquid, having a bitter-almond-like odor and a burning, aromatic taste." "Sparingly soluble in water (1:300); soluble in all proportions, in alcohol, ether, and fixed and volatile oils."

Synthetic benzaldehyde is usually prepared from benzylchloride or benzylidenechloride; unless carefully purified, such benzaldehyde will contain chlorinated products (hence the U. S. P. test for these: cf. also *Oleum Amygdalæ Amaræ*).

Unless properly prepared the benzaldehyde obtained from the natural oil of bitter almond may contain prussic acid (hence the U. S. P. test for this substance).

Benzaldehyde is the principal constituent of natural oil of bitter almond. The U. S. Pharmacopœia, Eighth Decennial Revision, demands that the official oil of bitter almond contain not less than 85 per cent of benzaldehyde. The natural oil of bitter almond also contains hydrocyanic acid; the Eighth Decennial Revision demands that the official oil contain not less than 2 per cent nor more than 4 per cent of hydrocyanic acid. The commercial natural oils of bitter almond contain from 1.5 to 11 per cent, or more, of hydrocyanic acid; hence (unless the hydrocyanic acid has been removed) they should be used with great caution as flavoring agents.

Dose.—"Average dose: 0.03 Cc. ($\frac{1}{2}$ minim)." (U. S. P.)

Caution.—It should be kept in small, amber-colored, well-stoppered bottles, as it is readily oxidized to benzoic acid; the latter change occurs more rapidly with the pure benzaldehyde than with the natural oil of bitter almond.

Nitrobenzene is an oil having an odor very much like that of oil of bitter almond; it is known as "artificial oil of bitter almond," or "essence of mirbane." It is sometimes used as a substitute for the oil of bitter almond in the manufacture of soap, cheap confectionery, etc. It is very poisonous.

BENZINUM PURIFICATUM.**Purified Petroleum Benzin.**

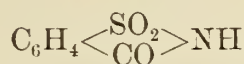
For certain purposes—as, for instance, the preparation of deodorized tincture of opium—the ordinary U. S. P. Benzinum (Petroleum Benzin or “petroleum ether”) is not sufficiently pure, hence the introduction of the purified product. The process of purification provided by the Pharmacopœia is designed to remove some of the heavier hydrocarbons and foreign, malodorous substances.

Petroleum ether is occasionally used in the preparation of mixtures for the production of general anæsthesia. Schleich has recommended three different mixtures for use in operations of short, moderate, and considerable duration, respectively:

	I.	II.	III.
Chloroform	45.0	45.0	30.0
Ether	180.0	150.0	80.0
Petroleum ether (boiling point 60–65° C.)	15.0	15.0	15.0
	$\underbrace{\hspace{1cm}}$	$\underbrace{\hspace{1cm}}$	$\underbrace{\hspace{1cm}}$
Boiling point of the mixture.....	38° C.	40° C.	42° C.

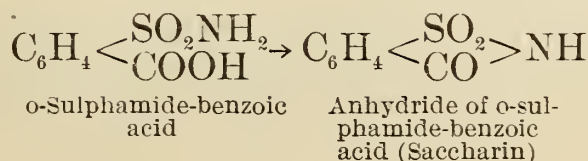
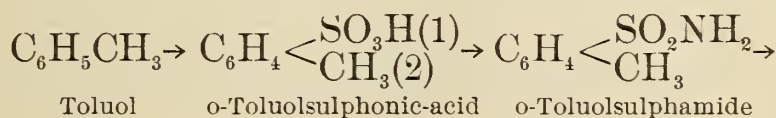
As Schleich’s theory turns entirely on the boiling point of the resulting mixture, it may be well to remember that the boiling point of Benzinum (U. S. P.) is given at 45°–60° C. Schleich’s mixtures are said, however, to have no constant boiling point.

(For other general anæsthetic mixtures, based upon Schleich’s researches, see under *Æthylis Chloridum*.)

BENZOSULPHINIDUM.**Benzosulphinide.****Saccharin.**

Official as Saccharinum in the Austrian and Swiss Pharmacopœias, as Glusidum (Gluside) in the British Pharmacopœia, and as Acide anhydroorthosulfamide-benzoïque in the French. It is variously known as *glucosimide*, *saccharol*, *saccharinol*, *saccharinose*, *agucarine*, etc.

Chemistry.—Chemically it is the anhydride of ortho-sulphamide-benzoic acid (benzoyl sulphonic-imide). Its derivation from toluol (from which it is usually made) is shown by the following formulas:



Saccharin was discovered in 1879 by Ira Remsen and C. Fahlberg.

Character.—A white, crystalline powder, nearly odorless, having an intensely sweet taste even in dilute solutions. The sweet taste may be recognized in a dilution of 1:100,000, as compared with cane sugar 1:200.

Solubility.—Soluble in 250 parts of water and in 25 parts of alcohol; more so in boiling water (1:24). It behaves like a strong acid and dissolves readily in alkalies; the sodium salt ($\text{C}_6\text{H}_4<\overset{\text{CO}}{\text{SO}_2}>\text{NNa}$) is known as *soluble saccharin* or *krystallose*.

The Liquor Saccharini of the National Formulary is a solution of saccharin in sodium bicarbonate and alcohol.

There are a number of preparations on the market, such as *antidiabeticin*, which contain saccharin.

Dose.—“Average dose: 0.200 Gm. = 200 milligrammes (3 grains).” (U. S. P.)

Dulcin or *sucrol*, another very sweet substance, is para-phenetolcarbamid; *Saxin* is a similar product.

BERBERIS.

Berberis.

The rhizome and roots of *Berberis aquifolium* and other species of Berberis. *Berberis aquifolium* is known as Oregon Grape Root. It contains an alkaloid, berberine, which is also found in Menispermum (a drug dropped from the present Revision), Calumba, Hydrastis, and other drugs.

A Fluidextract of Berberis has also been admitted into the U. S. Pharmacopœia.

Dose.—“Average dose: 2 Gm. (30 grains).” (U. S. P.)

BISMUTHI SUBGALLAS.

Bismuth Subgallate.

Official in the German Pharmacopœia as Bismutum subgallicum; also known as *dermatol*.

Composition.—Although somewhat variable in chemical composition, Bismuth Subgallate approximates the following formula: $\text{C}_6\text{H}_2(\text{OH})_3\text{CO}_2\text{Bi}(\text{OH})_2$, which contains 56.49 per cent of bismuth oxide (Bi_2O_3). The U. S. Pharmacopœia demands that it contain not less than 52 per cent, nor more than 57 per cent, of pure bismuth oxide.

Character.—An amorphous, bright yellow powder, odorless, tasteless, and permanent in the air.

Solubility.—Insoluble in water and alcohol, and in very dilute mineral acids. Readily soluble with decomposition in hydrochloric, nitric, and sulphuric acids, if these be heated. Alkalies dissolve it readily,

forming clear, yellow-colored solutions, which rapidly change to deep red.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

It is used in general for the same purposes as the subnitrate.

BISMUTHI SUBSALICYLAS.

Bismuth Subsaliolate.

Official under the names of Bismutum subsalicylicum (P. G.), Bismutum salicylicum (Swiss), Bismuthi Salicylas (Br. P.). The composition varies somewhat, but is approximately $C_6H_4(OH)CO_2BiO$. The U. S. Pharmacopœia requires that it yield not less than 62 per cent, nor more than 64 per cent, of pure bismuth oxide.

Character.—"A white, or nearly white, amorphous or crystalline powder, odorless, tasteless, and permanent in the air."

Solubility.—Almost insoluble in water; on prolonged boiling with water, a more basic salt is formed through the splitting off of free salicylic acid. Alcohol or ether extracts salicylic acid, with decomposition of the salt. Acids decompose it, with separation of a white, flocculent precipitate of salicylic acid.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

Other Unofficial Bismuth Compounds.—A large number of bismuth compounds have been proposed for medicinal use in the last few years. The following may be mentioned as examples: *Airol* (bismuth oxyiodo-subgallate), *bismal* (bismuth methylene digallate), *bismutol* ("bismuth sodium phosphate salicylate"), *crurin* (quinolin bismuth sulphocyanate), *eudorin* (bismuth tetraiodo-phenolphthalein), *iodogallicin* (bismuth oxyiodide methyl-gallol), *orphol* (bismuth betanaphthol), other phenolates, the benzoate, the chrysophanate (*dermol*), the cinnamylate (*hetoform*), the cresolate, the lactate, the bilactomonotannate (*lactanine*), the phenolsulphonate, the tannate, and similar salts; also proteid compounds, as the peptonate; compounds with resorcin, pyrogallol (*helcosol*), etc.

BROMOFORMUM.

Bromoform.



Official in the German Pharmacopœia as Bromoformium. This is tribrommethane, being entirely analogous in composition to chloroform and iodoform.

Character.—A heavy, transparent, colorless, mobile liquid having an ethereal odor and a penetrating, sweetish taste resembling chloroform.

Solubility.—Only slightly soluble in water, but readily in alcohol and ether. Specific gravity at 25° C., 2.808. It is only slightly volatile at ordinary temperature, boils at 148° C., and solidifies at 6° C.

Absolute bromoform is decomposed in presence of light and air more rapidly than chloroform. The addition of 4 per cent of alcohol, as in the case of chloroform, will preserve bromoform for months. When decomposed, bromine is set free, which colors the liquid yellowish red.

Dose.—"Average dose: 0.2 Cc. (3 minims)." (U. S. P.)

Caution.—Keep in dark amber-colored, glass-stoppered bottles in a cool place, protected from light.

CATAPLASMA KAOLINI.

Cataplasma of Kaolin.

Introduced in response to a request for an external clay preparation; similar to a number of commercial articles. The constituents are kaolin (57.7 per cent), boric acid, methyl salicylate, glycerin, and small quantities of thymol and oil of peppermint.

CERATUM RESINÆ COMPOSITUM.

Compound Rosin Cerate.

Composed of rosin, yellow wax, suet, turpentine, and linseed oil. For formula and method of preparation see U. S. Pharmacopœia.

Minor changes in the constituents, not however affecting the strength of the active ingredients, have been made in all the cerates with the exception of Ceratum Resinæ.

Ceratum Cantharidis, for instance, should no longer have the odor of oil of turpentine.

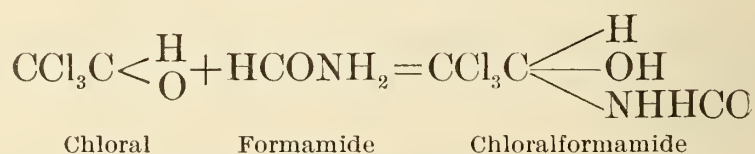
CHLORALFORMAMIDUM.

Chloralformamide.



Chloralum formamidatum (P. G.). Also known as *Chloralamide*, a name which, because it is both inaccurate and misleading (being properly applied to another substance), should not be used.

Chemistry.—It is formed by the direct union of anhydrous chloral and formamide, as shown by the following reaction:



Properties.—Colorless, lustrous crystals, odorless, and having a somewhat bitter taste.

Soluble in water (1:18.7) and alcohol (1:1.3), readily in glycerin and acetone. It is not affected by dilute acids, but is decomposed, on warming with alkali hydroxides, yielding chloroform; it behaves in this respect like chloral hydrate, and is, hence, incompatible with alkalies. Chloral is formed by its decomposition in the body; the formamide which is formed at the same time is supposed to stimulate the circulation and thus counteract the depression caused by the chloral.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

Caution.—Keep in amber-colored, well-stoppered bottles. It is easily decomposed in solution by heat; hence heat should not be used in preparing aqueous solutions. Avoid combination in full dose with other drugs of a similar physiologic action, for example, Sulphonethylmethane (*trional*), Sulphonmethane (*sulphonal*), Hydrated Chloral, etc.

Allied Compounds.—Chloral, like other aldehydes, forms many addition products more or less comparable with chloralformamide. Thus, with ethyl carbamate, chloral unites to form *uralium*; with dextrose it forms *chloralose*; with antipyrine, *hypnal*; with amylene hydrate, *dormiol*, etc.

Croton chloral (Butyl-chloral Hydras, Br. P.) is trichlorobutylaldehyde hydrate ($\text{CH}_3\text{CHClCCl}_2\text{CH}(\text{OH})_2$). Other tri-chlor substitution products recently proposed as hypnotics are *chloretone* or *aneson* (trichloropseudobutylalcohol or *acetone-chloroform*) and *isopral* (trichlorisopropyl alcohol).

CINNALDEHYDUM.

Cinnamic Aldehyde.



Obtained from oil of cinnamon or prepared synthetically. It is the chief and essential constituent of oil of cinnamon, and should be present to the extent of about 75 per cent by volume in a good oil.

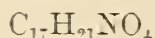
Character.—A colorless liquid, having a cinnamon-like odor and a burning, aromatic taste. It may be used for nearly all purposes in place of the official oil of cinnamon. Pure synthetic Cinnamic Aldehyde occurs in the market, and has, to a great extent, displaced the natural oil of cinnamon.

Solubility.—Sparingly soluble in water, readily in alcohol, fixed and volatile oils.

Dose.—"Average dose: 0.05 Cc. (1 minim)." (U. S. P.)

COCAINA.

Cocaine.



Official under same name in the British Pharmacopœia. An alkaloid obtained from several varieties of Coca. Hitherto only the most frequently used salt of Cocaine—the hydrochloride—was official in the U. S. Pharmacopœia.

Properties.—Slightly soluble in water (1:600), much more so in alcohol (1:5), more readily in both when warm: insoluble in glycerin.

Cocaine is a methyl compound of benzoylecgonine. When it is boiled with water methyl alcohol is first split off, then benzoic acid; these changes occur more rapidly with dilute acids or barium hydroxide. Conversely cocaine may be built up by introducing the methyl and benzoyl groups into ecgonine (a compound having the empirical formula $\text{C}_9\text{H}_{15}\text{NO}_3$).

Cocaine is contained in the newly introduced Oleatum Cocainæ.

Dose.—“Average dose: 0.030 Gm. = 30 milligrammes ($\frac{1}{2}$ grain).” (U. S. P.)

Substitutes for Cocaine.—A number of synthetic compounds with names suggestive of that of cocaine have recently been introduced as local anæsthetics. Among the best known of these are *beta-eucaine* (the hydrochloride of benzoyl-vinyl-diacetonealkamin); *holocaine*, which may be regarded as a derivative of acetphenetidin (*phenacetin*); *tropacocaine* (benzoylpseudotropein); *nirvanin*, *anæsthin* (para-amido-benzoic acid ester) and *orthoform*, complex derivatives of benzoic acid. *Stovain* is a recent addition to this group.

CODEINE PHOSPHAS.

Codeine Phosphate.



Official under same name in the British Pharmacopœia and as Codeinum phosphoricum in the German. Hitherto the free alkaloid alone was official in the U. S. Pharmacopœia.

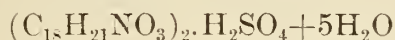
Character.—“Fine, white, needle-shaped crystals or crystalline powder, without odor, and having a bitter taste.”

Solubility.—Soluble in 2.25 parts of water, 261 parts of alcohol, more so when either is warmed. The aqueous solution has a slightly acid reaction to litmus.

Dose.—“Average dose: 0.03 Gm. = 30 milligrammes ($\frac{1}{2}$ grain).” (U. S. P.)

CODEINE SULPHAS.

Codeine Sulphate.



Character.—Long, glistening, white needles, prisms or crystalline powder, efflorescent in the air, odorless and having a bitter taste.

Solubility.—Soluble in about 30 parts of water and 1,035 parts of alcohol—much more so when either is warmed.

The aqueous solution is neutral to litmus paper.

Dose.—“Average dose: 0.030 Gm. = 30 milligrammes ($\frac{1}{2}$ grain).” (U. S. P.)

Similar Morphine Derivatives.—Codeine is methylmorphine ($C_{17}H_{18}(CH_3)NO_3$). *Dionine* is ethylmorphine hydrochloride ($C_{17}H_{17}NO(OH)OC_2H_5HCl + H_2O$). *Peronine* is benzylmorphine hydrochloride ($C_{17}H_{18}NO_3(C_6H_5CH_2)HCl$). *Heroine* is diacetylmorphine ($C_{17}H_{17}NO(C_2H_3O_2)_2$).

Syrupus Codeinæ, N. F. is a 1 per cent solution of Codeine Sulphate in Syrup.

COLCHICINA.

Colchicine.



An alkaloid obtained from *Colchicum*. The U. S. Pharmacopœia demands that the official *Colchici Cormus* contain not less than 0.35 per cent and the *Colchici Semen* not less than 0.55 per cent of colchicine. Although classed with the alkaloids, colchicine has an acid reaction.

Character.—Pale yellow leaflets or a pale yellow, amorphous powder, turning darker on exposure to light, having an odor suggesting damp hay and a very bitter taste.

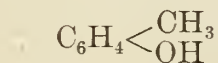
Solubility.—Soluble in water (1:22) and readily so in alcohol.

Incompatibility.—Colchicine is precipitated from solution by tannic acid.

Dose.—“Average dose: 0.0005 Gm. = 0.5 milligramme ($\frac{1}{128}$ grain).” (U. S. P.)

CRESOL.

Cresol.



A mixture of three isomeric cresols obtained from coal tar, freed from phenol, hydrocarbons, and water. Sometimes erroneously called cresylic acid. Cresol is methyl phenol, the three isomeric forms being known chemically as ortho-, meta-, and para-cresol.

Character.—A colorless or straw-colored refractive liquid having a phenol-like odor and turning yellowish-brown on prolonged exposure to light.

Solubility.—Soluble in water (1:60) and miscible in all proportions with alcohol and glycerin.

Miscible with alkali hydroxide solutions, forming alkali cresolates, homologous with alkali phenolates.

Purity.—"If 1 Cc. of cresol be mixed with 1 Cc. of glycerin, a clear solution should be produced, from which, on the addition of 1 Cc. of water, the cresol should completely separate (absence of, and distinction from, phenol)."

Dose.—"Average dose: 0.05 Cc. (1 minim)." (U. S. P.)

Much has been written concerning the germicidal and toxic properties of cresol. It is generally held that cresol is more toxic to bacteria than is phenol, but that it is less toxic to higher animals than is the latter. Tollens (Arch. f. exper. Path. u. Pharm., 52, p. 220; 1905) finds that para-cresol is more than twice as toxic for mice as is phenol, ortho-cresol has the same toxicity, while meta-cresol is less toxic. Thus the toxicity of a cresol will depend upon the relative proportion of the three constituents and these seem to vary in different preparations; Tollens finds some specimens to be more toxic than phenol. The U. S. Pharmacopœia does not specifically state the proportions in which the three cresols are present, although it fixes limits for the boiling point, specific gravity, and solubility. A preparation on the market under the name of *tricresol* (*enterol*) is said to contain 35 per cent of ortho-cresol, 40 per cent of meta-cresol, and 25 per cent of para-cresol; it is soluble to the extent of 2.2 to 2.55 per cent in water. The physiological action of the cresols is almost identical with that of phenol.

The cresols are constituents of coal tar and other crude antiseptic substances. Being but slightly soluble in water, they are often used in the form of emulsions or are dissolved with the aid of salts or of soap. The official *Liquor Cresolis Compositus* (q. v.) belongs to the latter class; it is practically identical with the *Liquor Cresoli saponatus* of the German Pharmacopœia and the preparation on the market known as *lysol*. The mixtures known as *creolins* usually contain impure cresol dissolved with the aid of rosin soap; they usually form emulsions when diluted with water. In *solveol* and *solutol* the cresols are held in solution by means of salts. A vast number of similar compounds are upon the market, usually under fanciful names.

Losophan and *europen* are iodine compounds of cresol. *Kresamine* is an aqueous solution of tricresol and ethylenediamine.

ELIXIR ADJUVANS.

Adjuvant Elixir.

This is made by the addition of Fluidextract of Glycyrrhiza to Aromatic Elixir. An excellent vehicle for bitter or nauseous remedies.

A somewhat similar elixir is to be found in the National Formulary under the same name.

ELIXIR FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM.

Elixir of Iron, Quinine and Strychnine Phosphates.

This is the official representative of a large class of popular preparations on the market; the formula is an improvement on a similar one in the National Formulary. (See also Glyceritum Ferri, Quininæ et Strychninæ Phosphatum). Some of the commercial elixirs bearing this name are said to contain no phosphoric acid.

Dose.—"Average dose: 4 Cc. (1 fluidrachm.)." (U. S. P.) Each fluidrachm contains 0.0647 Gm. (1 grain) of ferric phosphate, 0.0324 Gm. ($\frac{1}{2}$ grain) of quinine, and 0.001 Gm. ($\frac{1}{64}$ grain) of strychnine.

EMPLASTRUM ADHÆSIVUM.

Adhesive Plaster.

This is to take the place of Emplastrum Resinæ (U. S. P. 1890), from which it differs chiefly in the substitution of rubber for rosin. For formula and method of preparation see the Pharmacopœia.

EMULSUM OLEI MORRHUÆ.

Emulsion of Cod Liver Oil.

A standard official preparation, containing 50 per cent of cod liver oil, which might well replace many of the proprietary articles.^a It may be flavored, to suit the taste, with Oil of Gaultheria, Oil of Bitter Almond, etc.

Dose.—"Average dose: 8 Cc. (2 fluidrachms)." (U. S. P.)

EMULSUM OLEI MORRHUÆ CUM HYPOPHOSPHITIBUS.

Emulsion of Cod Liver Oil with Hypophosphites.

Similar to the above, but containing the hypophosphites of calcium, potassium, and sodium.

Dose.—"Average dose: 8 Cc. (2 fluidrachms)." (U. S. P.)

EMULSUM OLEI TEREBINTHINÆ.

Emulsion of Oil of Turpentine.

A 15 per cent (by volume) emulsion of rectified oil of turpentine, containing 5 per cent (by volume) of expressed oil of almond.

Dose.—"Average dose: 4 Cc. (1 fluidrachm)." (U. S. P.) One fluidrachm contains about 9 minims of oil of turpentine.

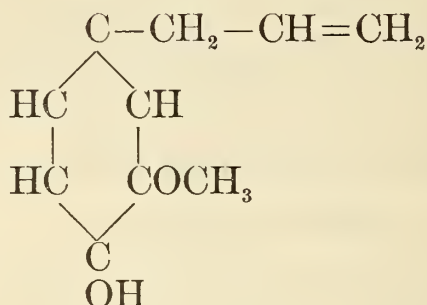
The National Formulary gives a somewhat similar preparation under the name of Emulsio Olei Terebinthinæ.

^a The character of some of these preparations is shown by the statement (Jour. Amer. Med. Assoc., 44, p. 1943; 1905) that a specimen of a "Tasteless Cod Liver Oil" contained no oil whatever.

EUGENOL.**Eugenol.**

An unsaturated, aromatic phenol obtained from Oil of Cloves and other sources.

Chemistry.—Chemically it is para-oxy-meta-methoxy-allyl-benzol having the formula:



Character.—A colorless, or pale yellow, thin liquid, highly refractive, and having a strongly aromatic odor of cloves and a pungent, spicy taste.

Solubility.—Almost insoluble in water, easily soluble in alcohol; should be soluble in 2 parts of 70 per cent alcohol.

This is the chief constituent of Oil of Cloves and may be used instead of the latter; it is also the chief constituent of Oil of Pimenta.

Dose.—"Average dose: 0.2 Cc. (3 minims)." (U. S. P.)

Caution.—It should be kept in well-stoppered amber-colored bottles, in a cool place, protected from light. Exposure to air causes the oil to become darker and thicker.

Derivatives.—Eugenol acetamide and eugenolcarbinol have been recommended as local anæsthetics and antiseptics; eugenol iodide is said to resemble aristol. *Benzeugenol* is the benzoic ether of eugenol.

EXTRACTUM MALTI.**Extract of Malt.**

This and Maltum (q. v.) are reintroductions into the Pharmacopœia of articles admitted to the 1880 revision but dismissed in 1890; it is contained in the National Formulary. Extractum Malti Fluidum, N. F., is a hydro-alcoholic extract.

Properties.—Malt extract consists of easily assimilable carbohydrates—maltose and dextrin—and small quantities of proteids; the ash contains the phosphates of calcium and magnesium. If the malt has not been overheated (by which the diastase would be destroyed), and if the extract is prepared according to the U. S. Pharmacopœia process, the preparation, when fresh, will contain diastase which is an efficient ferment for the conversion of starch into dextrose; the diastatic power, however, rapidly deteriorates on keeping.

Malt extract is contained in numerous infant foods and in malted milks. It is said that much glucose is frequently added to the malt extracts on the market. Many liquid "malt extracts" contain considerable quantities of alcohol, and are very similar to beer.

Dose.—"Average dose: 16 Cc. (4 fluidrachms)." (U. S. P.)

It should be kept in well-closed vessels in a cool place.

EXTRACTUM RHAMNI PURSHIANÆ.

Extract of Cascara Sagrada.

Also official in British Pharmacopœia. This solid extract and the Aromatic Fluidextract of Cascara Sagrada are two new preparations of the bark introduced into the Pharmacopœia. Formerly, only the fluid extract was official. One part of the solid extract represents the activity of four parts by weight of the bark.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.) This represents 1 Gm. (15 grains) of the bark and is equal to the Pharmacopœial dose of the fluidextract, namely, 1 Cc. (15 minims).

For a recent discussion of the chemistry of Cascara Bark see Jowett, Proc. Amer. Pharm. Assoc., 1904, p. 288.

EXTRACTUM SCOPOLE.

Extract of Scopolia.

This is prepared by evaporating, to a pilular consistence, the Fluidextract of Scopolia (q. v.). The latter is prepared from the rhizome of *Scopolia carniolica*, a plant closely related, in its characters and properties, to belladonna and hyoscyamus.

The U. S. Pharmacopœia demands that the extract of scopolia contain 2 per cent of mydriatic alkaloids; for method of assay see Pharmacopœia.

Dose.—"Average dose: 0.010 Gm. = 10 milligrammes ($\frac{1}{8}$ grain)." (U. S. P.)

EXTRACTUM SUMBUL.

Extract of Sumbul.

Prepared from the Fluidextract of Sumbul (q. v.).

In the U. S. Pharmacopœia 1890 the only preparation of Sumbul was the tincture; this is now dropped and the extract and fluidextract admitted.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

FLUIDEXTRACTA.

Fluidextracts.

In the 1890 Pharmacopœia the solid and the fluid extracts were grouped together; this resulted, at times, in confusion both as to

identity and strength of the several preparations. To avoid this, the new Pharmacopœia gives to the fluidextracts a new alphabetic position, grouping them by themselves; thus *Extractum Aconiti Fluidum* (U. S. P., 1890) becomes *Fluidextractum Aconiti* in the Eighth Decennial Revision. Wherever practicable, assay processes have been introduced, thus ensuring preparations of definite and uniform strength. Many of the solid extracts are directed by the Eighth Revision to be made from the fluidextracts.

Three fluidextracts, those of *Lobelia*, *Sanguinaria* and *Squill*, formerly made with alcohol or (*Sanguinaria*) with alcohol, acetic acid and water, are now made with hydro-acetic acid.

FLUIDEXTRACTUM BERBERIDIS.

Fluidextract of Berberis.

Prepared from *Berberis* (q. v.).

Dose.—"Average dose: 2 Cc. (30 minims)." (U. S. P.)

FLUIDEXTRACTUM EUONYMI.

Fluidextract of Euonymus.

The solid extract of *Euonymus*, which was already official, is now prepared from this fluidextract.

Dose.—"Average dose: 0.5 Cc. (8 minims)." (U. S. P.)

FLUIDEXTRACTUM GRANATI.

Fluidextract of Pomegranate.

Hitherto only the bark of the stem and root of *Granatum* (Pomegranate) has been official: it was often administered in the form of a decoction (official in the Br. P.), but this was very unpleasant to take, owing to the large amount of tannic acid present. A mixture of the tannates of the most important active constituents (four alkaloids) of *Granatum* has also been introduced under the name *Pelletierinæ Tannas* (q. v.).

Dose.—"Average dose: 2 Cc. (30 minims)." (U. S. P.)

FLUIDEXTRACTUM QUERCUS.

Fluidextract of Quercus.

Prepared from the official *Quercus* (*Quercus Alba*, U. S. P., 1890), the bark of the white oak. The medicinal properties depend upon the tannin contained in the bark.

Dose.—"Average dose: 1 Cc. (15 minims)." (U. S. P.)

FLUIDEXTRACTUM QUILLAJÆ.

Fluidextract of Quillaja.

The tincture of *Quillaja* (soapbark) was already official.

It has sometimes been proposed to use quillaja or one of its most important constituents (saponin) as an emulsifying agent for cod-liver

oil, etc.; in the present state of our knowledge such use would seem to be unjustifiable (see Keirle and Dunning, Proc. Amer. Pharm. Assoc., 52, p. 402).

Dose.—"Average dose: 0.2 Cc. (3 minims)." (U. S. P.)

This fluidextract is contained in the National Formulary.

FLUIDEXTRACTUM RHAMNI PURSHIANÆ AROMATICUM.

Aromatic Fluidextract of Cascara Sagrada.

This is the Aromatic Fluidextract of Cascara Sagrada of the National Formulary. It differs from the Fluidextract, which was already official, in having an aromatic flavor and being devoid of the intensely bitter principle occurring in the bark. It might well take the place of a number of commercial articles. The Extractum Rhamni Purshianæ (q. v.) is also a new introduction.

Dose.—"Average dose: 1 Cc. (15 minims)." (U. S. P.)

FLUIDEXTRACTUM SCOPOLE.

Fluidextract of Scopola.

Prepared from Scopola (q. v.) and containing 0.5 per cent of the mydriatic alkaloids of this drug. A method of assay is given in the U. S. Pharmacopœia.

Dose.—"Average dose: 0.05 Cc. (1 minim)." (U. S. P.)

This dose contains 0.00025 gram ($\frac{1}{256}$ grain) of the scopola alkaloids.

FLUIDEXTRACTUM STAPHISAGRIÆ.

Fluidextract of Staphisagria.

Prepared from the seeds, the official part, of *Delphinium staphisagria* (Stavesacre). Several bases have been described as occurring in stavesacre, but they may all be decomposition products of the aconitine-like alkaloid, delphinine.

Dose.—"Average dose: 0.05 Cc. (1 minim)." (U. S. P.)

FLUIDEXTRACTUM SUMBUL.

Fluidextract of Sumbul.

This and the Extract of Sumbul (q. v.) are new additions, while the tincture (U. S. P., 1890) is dropped.

Dose.—"Average dose: 2 Cc. (30 minims)." (U. S. P.)

GAMBIR.

Gambir.

This takes the place of Catechu of the Pharmacopœia of 1890. Catechu is an extract prepared from the wood of *Acacia catechu* (natural order Leguminosæ); Gambir is an extract prepared from the leaves

and twigs of *Uncaria gambir* (fam. Rubiaceæ.). Both drugs contain a large percentage of tannic acid and its compounds. Gambir was introduced on account of the difficulty of obtaining in the market true *Acacia catechu*. The *Tinctura Catechu Composita* and the *Trochisci Catechu* (U. S. P., 1890) are replaced by *Tinctura Gambir Composita* and *Trochisci Gambir*.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

GELATINUM.

Gelatin.

Official in the British Pharmacopœia under the same name; in the German as *Gelatina alba*. The U. S. Pharmacopœia demands that upon ignition it leave not more than 2 per cent of ash. Most of the gelatin on the market has an acid reaction.

GELATINUM GLYCERINATUM.

Glycerinated Gelatin.

A mixture of equal parts of gelatin and glycerin. The mass when cold is solid, but easily melts on applying gentle heat.

Basis for suppositories and bougies.

Of late years both ointments and cerates have been largely superseded, especially in Europe, by dermatologic pastes and glycerogelatins. The former are mixtures of the medicinal agents with starch, dextrin, or kaolin, and glycerin, soft soap, petrolatum, or lard, and are intended chiefly for antiseptic, astringent, or germicidal effects. The glycerogelatins are firmer than the pastes, and must be melted before they can be applied.

GLANDULE SUPRARENALES SICCE.

Desiccated Suprarenal Glands.

The cleaned, dried, and powdered suprarenal glands of the sheep or ox, freed from fat.

Properties.—A light, yellowish, amorphous powder, having a slight characteristic odor; partially soluble in water. One part of the dried glands represents approximately 6 parts of fresh glands.

Aqueous extracts of the glands rapidly deteriorate on keeping and should, therefore, be freshly prepared.

Dose.—"Average dose: 0.250 Gm.=250 milligrammes (4 grains)." (U. S. P.)

The blood-pressure raising constituent of the suprarenal glands is upon the market under the names *adrenephrin*, *adrenaline*, *epinephrine*, *epirenan*, *hemisine*, *paranephrin*, *suprarenalin*, *suprarenin*, etc.

GLANDULE THYROIDEÆ SICCE.

Desiccated Thyroid Glands.

The cleaned, dried, and powdered thyroid glands of the sheep, freed from fat.

A liquid preparation is official in the British Pharmacopœia.

Properties.—A yellowish amorphous powder, having a slight peculiar odor; partially soluble in water.

Dose.—“Average dose: 0.250 Gm.=250 milligrammes (4 grains).” (U. S. P.)

Numerous extracts of the thyroid are upon the market, many of them purporting to be the active constituent. *Aiodine*, *opothyroidine*, and *thyroglandine* are other preparations on the market.

Thyreoidectin and *rodagen* represent a new series of preparations quite recently introduced which must not be confused with the above; their action is stated to be exactly the opposite of that of the thyroid preparations. *Thyreoidectin* is prepared from the blood, *rodagen* from the milk, of animals from which the thyroids have been removed.

GLYCERITUM FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM.

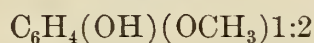
Glycerite of the Phosphates of Iron, Quinine and Strychnine.

This preparation is a concentrated form of one of the popular and useful combinations of tonics which might well replace some of the many commercial articles; it is prepared according to a fixed and definite formula (see U. S. P.), whereas the latter class are made according to the special formulæ of the different manufacturers. (See also Elixir Ferri, Quininæ et Strychninæ Phosphatum.) This glycerite is a stable solution which may be kept in stock, and from which the Syrup of the Phosphates of Iron, Quinine and Strychnine may readily be prepared.

Dose.—“Average dose: 1 Cc. (15 minims).” (U. S. P.) 1 Cc. contains 0.080 Gm.=80 milligrammes ($1\frac{1}{4}$ grains) of soluble ferric phosphate, 0.104 Gm.=104 milligrammes ($1\frac{3}{5}$ grains) of quinine, and 0.0008 Gm.=0.8 milligrammes ($\frac{1}{80}$ grain) of strychnine. The ratio of quinine to strychnine is four times as great in the glycerite as in the elixir.

GUAIACOL.

Guaiacol.



One of the chief constituents of creosote; prepared either from beechwood tar, or synthetically. Chemically it is the monomethyl ether of pyrocatechin (orthodihydroxy-benzene).

Character.—Either a clear, colorless or light yellow, oily fluid, or colorless, prismatic crystals, which melt at 28.5°C . It has an agreeable, aromatic odor.

Solubility.—Soluble in water (1:53), glycerin (1:1), and easily in alcohol. Being phenolic in character, it readily dissolves in caustic alkalies and forms salts with a large number of acids, one of which (the carbonate) has been made official.

Of late years creosote has been largely superseded by guaiacol, upon which the value of creosote no doubt depends.

Dose.—"Average dose: 0.5 Cc. (8 minims)." (U. S. P.)

Caution.—It should be preserved in dark, amber-colored bottles, protected from the light. Guaiacol which has become dark from exposure to light may be rendered colorless by redistillation. To be used cautiously with other drugs of similar physiologic action, e. g., Creosotum, Resorcinol, Phenylis Salicylas, etc.

GUAIACOLIS CARBONAS.

Guaiacol Carbonate.



A guaiacol derivative obtained by the action of carbonyl chloride upon sodium-guaiacolate.

Also known as *duotal*.

Character.—A white, crystalline, neutral powder, nearly odorless and tasteless.

Solubility.—Insoluble in water; soluble in cold (1:48), more so in hot, alcohol; slightly soluble in glycerin and fatty oils.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

Other Guaiacol Compounds.—Numerous combinations of guaiacol with other acids, etc., are in the market, such as the benzoate (*benzosol*), benzyl-guaiacol, cacodylate (*cacodyliacol*), cinnamate (*styracol*), phosphate, salicylate (*guaiacol-salol*), sulphonate, valerianate (*gepsot*), etc.

HAMAMELIDIS CORTEX.

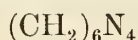
Hamamelis Bark.

Both the bark and twigs, and the leaves of *Hamamelis virginiana* are now recognized by the Pharmacopœia; the former are introduced under the above title and the old Hamamelis (U. S. P., 1890) becomes Hamamelidis Folia.

Dose.—"Average dose: 2 Gm. (30 grains)." (U. S. P.)

HEXAMETHYLENAMINA.

Hexamethylenamine.



A condensation product of formaldehyde and ammonia. Chemically it is hexamethylene-tetramine. Also known as *aminoform*, *ammonio-formaldehyde*, *cystamine*, *cystogen*, *formin*, *uritone*, and *urotropin*.

Character.—Colorless, lustrous, odorless crystals, having a sweetish, then somewhat bitter, taste. Its aqueous solution has an alkaline reaction to litmus.

Solubility.—Easily soluble in water (1:1.5), less so in alcohol (1:10).

In solution it is decomposed by dilute sulphuric acid with liberation of formaldehyde; it is precipitated by tannic acid and mercuric chloride.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

Caution.—It should be kept in well-stoppered bottles.

Allied Compounds.—Hexamethylene-tetramine readily forms compounds with a large number of substances; among those suggested for use in medicine the following may be mentioned:

Hexamethylenamine salicylate, *urotropin salicylate*, or *saliformin*; a colorless, crystalline powder of nauseous, sweetish, astringent taste.

Hexamethylenamine-ethylbromide, *bromalin*, or *bromoformin*; a colorless, crystalline powder of a sweetish saline taste.

Hexamethylenamine-tannin, *tannopin*, or *tannon*; a brown tasteless powder, nearly insoluble in water and alcohol.

Dioxybenzol-hexamethylenamine, *hetralin*, contains 60 per cent of hexamethylenamine.

Chinotropin and *chiniformin* are quimates of hexamethylenamine. *Helmitol* is a recently introduced compound of hexamethylenamine with anhydromethylene citric acid. *Citarin* (sodium anhydromethylene citrate) is another compound from which formaldehyde is split off in the organism.

HOMATROPINÆ HYDROBROMIDUM.

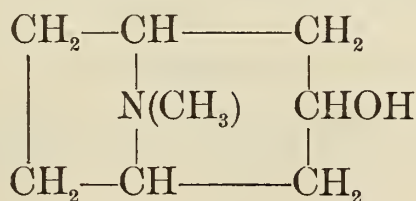
Homatropine Hydrobromide.



Official under the same name in the British Pharmacopœia; as Homatropinum hydrobromicum in the German and Swiss Pharmacopœias.

"The hydrobromide of an alkaloid obtained by the condensation of tropine and mandelic acid."

Chemistry.—Atropine may be broken up, by the action of alkalies, into an alkaloid, tropine, and an aromatic acid, tropic acid. Tropine is a pyridine derivative having the structural formula



Tropine forms ester-like compounds with many acids; the compounds with aromatic acids are called tropeins. Homatropine is one of these tropeins; as stated above, it is formed by the union of tropine and mandelic acid; the latter is phenylglycollic acid ($\text{C}_6\text{H}_5\text{CH} < \begin{smallmatrix} \text{OH} \\ \text{COOH} \end{smallmatrix}$).

Tropic acid (the acid of atropine) is phenylhydracrylic acid ($\text{C}_6\text{H}_5\text{CH} < \begin{smallmatrix} \text{CH}_2\text{OH} \\ \text{COOH} \end{smallmatrix}$). Scopolamine (hyoscyne) is formed by the union of tropic acid with scopoline, a compound similar to tropine.

Properties.—Small, colorless, odorless, rhombic crystals or crystalline powder, having a bitter taste. Soluble in 5.7 parts of water and 32.5 parts of alcohol. It should be kept in well-stoppered vials protected from light.

Dose.—“Average dose: 0.0005 Gm. = 0.5 milligramme ($\frac{1}{128}$ grain).” (U. S. P.)

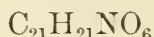
The physiological action of homatropine is similar to that of atropine, but it is less poisonous. The mydriatic effects of homatropine appear more quickly and pass off in a shorter time than do those of atropine.

The hydrochloride, sulphate, and salicylate of homatropine have been used, but they seem to have no advantage over the hydrobromide.

Euphthalmin is a recently introduced mydriatic, having a physiological action very similar to homatropine; it is a mandelic acid derivative of *beta-eucaine*.

HYDRASTINA.

Hydrastine.



An alkaloid obtained from *Hydrastis*. The U. S. Pharmacopœia, Eighth Decennial Revision, demands that *Hydrastis* contain not less than 2.5 per cent of Hydrastine. *Hydrastis* contains also the alkaloids berberine to the extent of 3.5 to 5 per cent, and canadine, but its physiological action is due largely to the Hydrastine. Hydrastine is frequently called in commerce the “white alkaloid of *hydrastis*.”

The alkaloid hydrastinine (the hydrochloride of which is official) is obtained from Hydrastine by the action of oxidizing agents. The alkaloid Hydrastine should not be confused with the mixture of hydrastine, berberine, etc., sold under the same name.

Properties.—“White, to creamy white, glistening prisms, sometimes of large size, possessing a bitter taste, and permanent in the air.” Almost insoluble in water; soluble in 135 parts of alcohol.

“If a crystal of Hydrastine be dissolved in diluted sulphuric acid and a solution of potassium permanganate (1 in 10) be added, a blue fluorescence will be developed (distinction from hydrastinine).”

Dose.—“Average dose: 0.010 Gm. = 10 milligrammes ($\frac{1}{3}$ grain).” (U. S. P.)

Hydrastine is extensively used in preparing the so-called “colorless *hydrastis*,” which is a solution of the alkaloid, in a mixture of water and glycerin, with the aid of hydrochloric or sulphuric acid.

IODOLUM.

Iodol.



Tetraiodopyrrol, a derivative of the base pyrrol ($\text{C}_4\text{H}_5\text{N}$) obtained by the direct action of iodine upon the base in the presence of alcohol.

Properties.—A light, grayish-brown, crystalline powder without odor or taste. Very slightly soluble in water (1:4900), much more so in alcohol (1:9); soluble in fixed oils.

Dose.—“Average dose: 0.250 Gm.=250 milligrammes (4 grains).” (U. S. P.)

This is one of the vast number of compounds proposed in the last few years as substitutes for iodoform. The iodine of iodol is apparently less easily split off the molecule than that of iodoform, and it is said to be less liable to produce poisoning.

Other iodine compounds.—Among the enormous number of other iodine compounds proposed as substitutes for iodoform may be mentioned: Thymolis Iodidum (U. S. P., Eighth Decennial Revision, commonly known as *aristol*); *airol* (bismuth oxy-iodo-gallate, with 20 per cent of iodine); *sanoform* (diiodo-methylsalicylate); the potassium, sodium, mercury, and zinc salts of *sozoiodolic acid* (phenol-sulphonic acid in which two atoms of hydrogen have been substituted by two atoms of iodine— $\text{C}_6\text{H}_2\text{I}_2<\overset{(\text{OH})}{\text{SO}_2\text{OH}}$), known as *sozoiodolates*; *nosophen*, *antinosine*, and *eudoxine* (all iodine compounds of phenolphthalein); *losophan* and *europen* (combinations of cresol and iodine); *loretin* and *vioform* (derivatives of quinoline containing iodine); *diiodoform* (tetraiodoethylene, C_2I_4); sodium diiodosalicylate; acetone iodide; iodoso-benzoic acid, etc.

Various mixtures of iodoform and other substances have been made with the object of concealing the odor of the former; thus, *eka-iodoform* is said to consist of iodoform and paraformaldehyde; *anozol* of iodoform and thymol; *iodoformin* of iodoform and hexamethylene tetramine, etc. *Iodoformogen* is a proteid compound of iodoform. Iodoformum Aromaticum, N. F., is a mixture of iodoform and coumarin.

KAOLINUM.

Kaolin.

Official in the British Pharmacopœia under same name. A native aluminum silicate, consisting largely of the pure silicate $\text{H}_2\text{Al}_2\text{Si}_2\text{O}_8 + \text{H}_2\text{O}$. It is a very pure clay.

Properties.—Soft, white or yellowish-white powder, odorless, and having an earthy or clay-like taste.

Insoluble in water.

Kaolin is contained in Cataplasma Kaolini (q. v.). It is used in dusting powders: also in pills containing easily reduced bodies, such as silver nitrate or potassium permanganate, which can not be mixed with ordinary excipients.

LIQUOR ANTISEPTICUS.

Antiséptic Solution.

A solution of mild aromatics and antiseptics similar to certain commercial preparations. Among other things it contains about 2 per cent of boric acid, 0.1 per cent each of benzoic acid and thymol, and 25 per cent of alcohol.

Dose.—"Average dose: 4 Cc. (1 fluidrachm)." (U. S. P.)

LIQUOR CHLORI COMPOSITUS.

Compound Solution of Chlorine.

Chlorine Water.

This takes the place of Aqua Chlori (U. S. P., 1890). The method of preparation (for which see the Pharmacopœia) is materially changed and simplified. When freshly prepared it contains about 0.4 per cent of chlorine with some oxides of chlorine and potassium chloride.

Dose.—"Average dose: 4 Cc. (1 fluidrachm)." (U. S. P.)

LIQUOR CRESOLIS COMPOSITUS.

Compound Solution of Cresol.

Liquor Cresoli saponatus is the official German title of a somewhat similar preparation. It is essentially a linseed-oil-soap solution of cresol, of 50 per cent strength; the soap dissolves the cresol as do alkalies. This is a mixture of much more definite composition than many commercial preparations of similar nature.

For practical use the 50 per cent solution is diluted with water to various degrees according to need.

Other preparations of this nature are known as *creolin*, *disinfectol*, *enterocresol*, *germol*, *cresolin*, *lysol*, *lysitol*, etc. (See Cresol).

LIQUOR FORMALDEHYDI.

Solution of Formaldehyde.

An aqueous solution containing not less than 37 per cent by weight of absolute Formaldehyde (H.CO.H); an assay process is provided. Official in the German Pharmacopœia as Formaldehydum solutum and variously known as *formalin*, *formol*, *methylaldehyde*, *oxymethylene*, *methanal*, etc.

Properties.—Formaldehyde itself is a gas at ordinary temperatures having a very pungent odor. The various products on the market are solutions of the gas in water. Formaldehyde readily undergoes a

molecular change called polymerization, whereby a solid form is obtained, known as paraformaldehyde or simply *paraform*. When a solution of formaldehyde is evaporated by heat, and more slowly by long standing, paraformaldehyde separates as a white, flocculent, nearly odorless mass, which is almost insoluble in water, alcohol, or ether, and which begins to sublime below 100° C. When heated, paraformaldehyde vaporizes and reforms the gaseous formaldehyde. It occurs in the market in tablets which are employed for disinfecting purposes.

Formaldehyde is very active chemically; it has a strong reducing action on silver, copper, and mercury salts, and unites readily with ammonia, forming the official odorless Hexamethylenamine (which see). It is easily oxidized by hydrogen dioxide and potassium permanganate, especially in alkaline solution.

Several dusting powders containing formaldehyde, in combination, have been introduced; thus, *glutol* is a compound of gelatin and formaldehyde, *amyloform*, of starch and formaldehyde, etc.

Formaldehyde is a constituent of many food preservatives, embalming preparations, etc.

Caution.—Keep well stoppered in a moderately cool place and protected from light.

LIQUOR SODII PHOSPHATIS COMPOSITUS.

Compound Solution of Sodium Phosphate.

A fairly stable concentrated solution containing 1 Gm. of Sodium Phosphate in each Cc.

Dose.—“Average dose: 8 Cc. (2 fluidrachms).” (U. S. P.)

Keep well stoppered and moderately warm.

MAGNESII SULPHAS EFFERVESCENS.

Effervescent Magnesium Sulphate.

A similar compound is official under the same name in the British Pharmacopœia; known also as effervescent Epsom salt, and as magnesii sulphas granulatus.

This may take the place of Magnesii Citras Effervescens (U. S. P., 1890), which has been dropped.

Dose.—“Average dose: 16 Gm. (240 grains).” (U. S. P.)

MALTUM.

Malt.

This is a reintroduction; Maltum was official in the U. S. Pharmacopœia, 1880, but was dropped in 1890. Used for the preparation of Extractum Malti (q. v.).

MANGANI DIOXIDUM PRÆCIPITATUM.

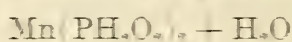
Precipitated Manganese Dioxide.

To replace Mangani Dioxidum, U. S. Pharmacopœia, 1890. It consists chiefly of manganese dioxide (MnO_2), with small amounts of other oxides of manganese, corresponding to not less than 80 per cent of manganese dioxide. The Mangani Dioxidum (1890) was the native crude manganese dioxide and was only required to contain at least 66 per cent of the pure dioxide.

Dose.—“Average dose: 0.250 Gm. = 250 milligrammes ($\frac{1}{4}$ grains).” (U. S. P.)

MANGANI HYPOPHOSPHIS.

Manganese Hypophosphite.



It should contain not less than 97 per cent of pure manganese hypophosphite.

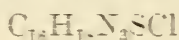
Dose.—“Average dose: 0.200 Gm. = 200 milligrammes (3 grains).” (U. S. P.)

It is contained in Syrupus Hypophosphitum Compositus.

METHYLTHIONINE HYDROCHLORIDUM.

Methylthionine Hydrochloride.

Methylene Blue.



Chemically, it is tetramethylthionine hydrochloride.

Properties.—Dark, green, crystalline powder, or prismatic crystals having a bronze-like luster.

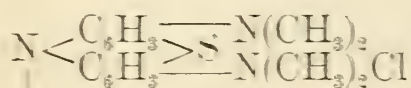
Readily soluble in water, somewhat less so in alcohol; the solutions are of a deep blue color.

Incompatible with potassium iodide. Reducing agents decolorize it.

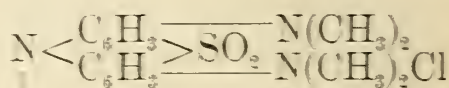
Dose.—“Average dose: 0.250 Gm. = 250 milligrammes ($\frac{1}{4}$ grains).” (U. S. P.)

Caution.—Not to be confounded with commercial methylene blue, which is often the zinc chloride double salt of tetramethylthionine, is employed as a dye or stain, and is unfit for internal administration.

Methylene azure, a dye which has recently come into prominence as a stain in histology (Romanowsky's stain, for example, depends upon the methylene azure present in “ripened” methylene blue), is derived from methylene blue by the addition of two atoms of oxygen to the sulphur.



Methylene blue



Methylene azure (chloride)

Methylene azure is almost always present in even the best specimens of methylene blue. It may be detected by adding ammonia to a solution of methylene blue and then shaking with ether; the methylene azure passes into the ether, which is colored red.

OLEATA.

Oleates.

Three new oleates have been introduced and one (*Oleatum Zinci*, U. S. P., 1890) dropped.

For method of preparation see the *Pharmacopœia*.

The oleate of quinine is also in the National Formulary; other (unofficial) oleates in the National Formulary are: oleate of aconitine, lead oleate, and zinc oleate (different from the U. S. P. 1890 Oleate of Zinc).

OLEATUM ATROPINÆ.

Oleate of Atropine.

Containing 2 per cent of atropine.

OLEATUM COCAINÆ.

Oleate of Cocaine.

Containing 5 per cent of cocaine.

OLEATUM QUININÆ.

Oleate of Quinine.

Containing 25 per cent of quinine.

OPIUM GRANULATUM.

Granulated Opium.

Opium dried at a temperature not exceeding 85° C. and reduced to a coarse (No. 20) powder; *Opii Pulvis* is prepared similarly, but it is reduced to a very fine powder; the *Pharmacopœia* requires that it contain not less than 12 per cent nor more than 12.5 per cent of crystallized morphine when assayed by the pharmacopœial process; the powdered and deodorized opium are also required to contain this percentage of crystallized morphine.

The Tincture of Opium is now made from granulated opium instead of from powdered opium, as in the U. S. *Pharmacopœia*, 1890. Much of the tincture of opium on the market seems to be under strength; it is hoped that a more uniform product will be obtained by the use of granulated opium.

Dose.—“Average dose: 0.065 Gm. = 65 milligrammes (1 grain).” (U. S. P.)

PARAFFINUM.**Paraffin.**

A mixture of solid hydrocarbons, chiefly of the methane series. The paraffin of the U. S. Pharmacopœia melts between 51.6° and 57.2° C. The "hard paraffin" (Paraffinum Durum) of the British Pharmacopœia melts between 54.4° and 57.2° C., while the "Paraffinum solidum" of the German Pharmacopœia melts between 74° and 80° C.

PELLETIERINÆ TANNAS.**Pelletierine Tannate.**

"A mixture in varying proportions of the tannates of four alkaloids (punicine, iso-punicine, methyl-punicine, and pseudo-punicine) obtained from *Punica granatum*" (Pomegranate). Also known as punicinum tannicum. The alkaloids are also known as pelletierine, iso-pelletierine, etc.

Character.—A yellowish-white, odorless, amorphous powder, having an astringent taste, and a weak acid reaction.

Solubility.—Soluble in water (1:235), alcohol (1:12.6), and in warm dilute acids.

Dose.—"Average dose: 0.250 Gm.=250 milligrammes (4 grains)." (U. S. P.)

The pelletierines of commerce seem to vary greatly; some are ten times as poisonous as others. While the U. S. Pharmacopœia names, as the average dose of the tannate, 0.25 Gm., some writers recommend 0.75 to 1.5 Gm. Very unpleasant effects are said to have resulted from 0.4 to 0.5 Gm.

PETROLATUM ALBUM.**White Petrolatum.**

"A white unctuous mass of about the consistency of an ointment." It is purified petrolatum and is used in the preparation of the Ointment of Boric Acid, the Ointment of Phenol (Unguentum Acidi Carbolici, U. S. P., 1890), etc.

PHENOL LIQUEFACTUM.**Liquefied Phenol.**

Practically the Acidum Carbolicum Liquefactum of the British and German Pharmacopœias. It is prepared from Phenol (Acidum Carbolicum, U. S. P., 1890) by the addition of distilled water in the proportion of 1 Gm. of the latter to 9 Gm. of Phenol. The U. S. Pharmacopœia Phenol must contain not less than 96 per cent of absolute phenol; whereas this preparation, Phenol Liquefactum, contains not less than 86.4 per cent, by weight, of absolute phenol and about 13.6

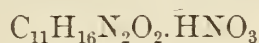
per cent. by weight, of water. Introduced on account of the ease of dispensing.

1 Gm. of Phenol (U. S. P.) equals about 1.11 Gm. of Liquefied Phenol, or 1 Gm. Liquefied Phenol equals about 0.9 Gm. of Phenol.

Dose.—"Average dose: 0.05 Cc. (1 minim)." (U. S. P.)

PILOCARPINE NITRAS.

Pilocarpine Nitrate.



This is the only salt of pilocarpine official in the British Pharmacopœia. The revised U. S. Pharmacopœia contains two salts of pilocarpine; the Pilocarpinæ Hydrochloras (U. S. P., 1890) is retained under the name of Pilocarpinæ Hydrochloridum, and the nitrate is introduced.

Character.—Colorless, or white, shining crystals, odorless, and having a faintly bitter taste. It is permanent in the air, whereas the hydrochloride is deliquescent on exposure to the air.

Solubility.—Soluble in water (1:4), alcohol (1:60), in warm alcohol (1:16). The aqueous solution (1 in 100) is acid to litmus.

Dose.—"Average dose: 0.010 Gm. = 10 milligrammes ($\frac{1}{5}$ grain)." (U. S. P.)

PILULÆ LAXATIVE COMPOSITE.

Compound Laxative Pills.

An official preparation which may well replace a number of similar commercial articles.

Each pill contains 0.013 Gm. = 13 milligrammes ($\frac{1}{5}$ grain) Aloin, 0.0005 Gm. = 0.5 milligramme ($\frac{1}{200}$ grain) Strychnine, 0.008 Gm. = 8 milligrammes ($\frac{1}{8}$ grain) Extract of Belladonna Leaves, and 0.004 Gm. = 4 milligrammes ($\frac{1}{25}$ grain) of Ipecac.

Dose.—"Average dose: 2 pills." (U. S. P.)

Pilulæ Aloini, Strychninæ et Belladonnæ, N. F., contain, with the exception of the Ipecac, the same active ingredients and in the same proportions.

PILULÆ PODOPHYLLI, BELLADONNÆ ET CAPSICI.

Pills of Podophyllum, Belladonna and Capsicum.

Each pill contains 0.016 Gm. = 16 milligrammes ($\frac{1}{4}$ grain) Resin of Podophyllum, 0.008 Gm. = 8 milligrammes ($\frac{1}{8}$ grain) Extract of Belladonna Leaves, and 0.032 Gm. = 32 milligrammes ($\frac{1}{2}$ grain) Capsicum.

Dose.—"Average dose: 1 pill." (U. S. P.)

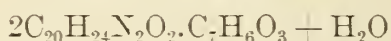
The same pill is included in the National Formulary under the same name.

PULVIS ACETANILIDI COMPOSITUS.**Compound Acetanilide Powder.**

A mixture of Acetanilide, Caffeine, and Sodium Bicarbonate; it is a modification of the National Formulary article of the same name and has been known as Acetanilid Compound (Aulde). The sodium bicarbonate increases the solubility of the acetanilide.

Dose.—"Average dose: 0.500 Gm. = 500 milligrammes ($7\frac{1}{2}$ grains)." (U. S. P.)

Acetanilide is the cheapest of the common antipyretics and it is extensively used in the "headache powders" sold under such a variety of names. These powders frequently contain also caffeine and an alkaline salt, usually sodium bicarbonate or ammonium carbonate. (For analyses of a number of these powders see Jour. Amer. Med. Assoc., Vol. 44, p. 1790, 1905.)

QUININE SALICYLAS.**Quinine Salicylate.**

Character.—Colorless needles, permanent in air, but acquiring a pinkish tinge after a time.

Solubility.—Soluble in cold water (1:77), somewhat more so in warm (1:35), in alcohol (1:11), and in glycerin (1:16).

It contains 68.79 per cent Quinine (the Bisulphate contains 59.1 per cent Quinine, the Hydrobromide 76.6 per cent, the Hydrochloride 81.8 per cent, the Sulphate 74.3 per cent). The Bisulphate is soluble in 5.5 parts of water, the Hydrobromide in 40 parts, the Hydrochloride in 18 parts, the Sulphate in 720 parts; the official alkaloid (containing 3 molecules of water) is soluble in 1,550 parts of water.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

SABAL.**Sabal.**

The partially dried ripe fruit of *Serenoa serrulata*, commonly known as saw palmetto.

Not much is known concerning the active principles of this drug, and there seems to have been no satisfactory investigation of its physiological action. Coblenz found in the pulp of the berries a volatile oil, a fixed oil, a fat, an alkaloid, a resin, dextrin, and glucose.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

SAFROLUM.

Safrol.



“The methylene ether of allyl pyrocatechol, found in oil of sassafras, camphor oil,” etc.

Properties.—A colorless, or faintly yellow, liquid with a sassafras-like odor. Soluble in about its own volume of strong alcohol and in about 30 volumes of 70 per cent alcohol.

Safrol is contained to the extent of 80 per cent in the official oil of sassafras (*Oleum Sassafras*). Much of the safrol of commerce is obtained from camphor oil. Safrol is used to a considerable extent in flavoring drinks (*sarsaparilla waters*) and perfuming soaps. Heffter (*Arch. f. exp. Path. u. Pharm.*, 35, p. 354) considers safrol to be the most poisonous of the volatile oils, and thinks its widespread use not unattended with danger. The effects of chronic poisoning are similar to those of yellow phosphorus.

Dose.—“Average dose: 0.3 Cc. (5 minims).” (U. S. P.)

SCOPOLA.

Scopola.

The dried rhizome of *Scopola carniolica*, Jacquin (Fam. *Solanaceæ*). Scopola is closely related to Belladonna and Hyoscyamus.

The Pharmacopœia demands that the drug contain not less than 0.5 per cent of alkaloids; it is assayed by the same process as are belladonna leaves.

Preparations admitted into the U. S. Pharmacopœia, Eighth Decennial Revision: Extract of Scopola and Fluidextract of Scopola (q. v.)

Dose.—“Average dose: 0.045 Gm. = 45 milligrammes ($\frac{3}{4}$ grain).” (U. S. P.)

The alkaloid of Scopola is almost wholly hyoscyamine. The content of the alkaloids in Scopola is remarkably uniform (about 0.55 per cent), whereas the percentage of alkaloids in Belladonna varies from 0.2 to above 1 per cent.

There has been much discussion as to how far Scopola can replace Belladonna in therapeutics; its preparations are said to be used extensively in the manufacture of “belladonna plasters.”

SCOPOLAMINE HYDROBROMIDUM.

Scopolamine Hydrobromide.



“The hydrobromide of an alkaloid obtained from plants of the *Solanaceæ*; chemically identical with Hyoscine Hydrobromide.”

Although Hyoscine Hydrobromide, which was admitted into the U. S. Pharmacopœia, 1890, and Scopolamine Hydrobromide are iden-

tical, both names are used in the U. S. Pharmacopœia, Eighth Decennial Revision, as separate headings, because most people are familiar with the name Hyoscine but not with Scopolamine. Scopolamine is formed by the union of tropic acid with scopoline, a compound similar to tropine. (See Homatropine.)

In the British Pharmacopœia Scopolamine Hydrobromide is used as a synonym for Hyoscine Hydrobromide; in the German Pharmacopœia only the name Scopolaminum hydrobromicum is retained.

Dose.—"Average dose: 0.0005 Gm. = 0.5 milligramme ($\frac{1}{2000}$ grain)." (U. S. P.)

SERUM ANTIDIPHTHERICUM.

Antidiphtheric Serum.

Diphtheria Antitoxin.

"A fluid separated from the coagulated blood of a horse immunized through the inoculation of diphtheric toxin."—U. S. Pharmacopœia. The German Pharmacopœia recognizes also the dried serum.

Antidiphtheric serum gradually loses its power, the loss in one year varying between 10 and 30 per cent.

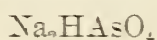
"The standard of strength, expressed in units of antitoxic power, should be that approved or established by the U. S. Public Health and Marine-Hospital Service." (U. S. P.) All manufacturers selling diphtheria antitoxin in the District of Columbia, or in States other than the one in which it is manufactured, must secure a license issued by the Secretary of the Treasury on recommendation of the Surgeon-General of the Public Health and Marine-Hospital Service. (For a full discussion of the official standard, see Rosenau, M. J.: The immunity unit for standardizing diphtheria antitoxin, Bulletin No. 21, Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service, 1905.)

Dose.—"Average dose: 3,000 units. Immunizing dose for well persons: 500 units." (U. S. P.)

Caution.—Should be kept in sealed glass containers in a dark place at temperatures between 4.5° and 15° C. (40° and 59° F.).

SODII ARSENAS EXSICCATUS.

Exsiccated Sodium Arsenate.



This is the same as the Sodii Arsenas of the British Pharmacopœia; also known as anhydrous sodium arsenate.

Properties.—An amorphous, odorless, white powder. Permanent in dry air. Soluble in 3 parts of water; very soluble in boiling water.

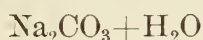
This is prepared from Sodium Arsenate (already official) by expelling by heat the seven molecules of water of the latter. The hydrous sodium arsenate (Sodii Arsenas, U. S. P.) is efflorescent in dry air

and somewhat deliquescent in moist air; hence the percentage of arsenic is somewhat uncertain. The new preparation is permanent in dry air. The hydrous sodium arsenate contains 40.4 per cent of water; hence, a given weight of this substance will contain but little more than half as much arsenic as an equal weight of the exsiccated. The average dose of the latter is accordingly placed at about one-half that of the former.

Dose.—"Average dose: 0.003 Gm. = 3 milligrammes ($\frac{1}{20}$ grain)." (U. S. P.)

SODII CARBONAS MONOHYDRATUS.

Monohydrated Sodium Carbonate.



Sodii Carbonas and Sodii Carbonas Exsiccatus (U. S. P., 1890) are dismissed from the Pharmacopœia and the monohydrated salt introduced.

The Sodii Carbonas contained ten molecules of water of crystallization or 63 per cent; part of this was lost on exposure to air, so that the salt was of uncertain strength. The Sodii Carbonas Exsiccatus contained about 26 per cent of water and probably corresponded to the formula $\text{Na}_2\text{CO}_3 + 2\text{H}_2\text{O}$. This salt was somewhat hygroscopic. The monohydrated salt does not effloresce at ordinary temperatures, nor does it absorb much moisture. It is therefore more uniform in composition than either of the others.

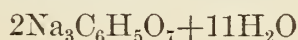
Character.—A white, crystalline, granular powder, odorless and having a strong alkaline taste. It is somewhat less soluble than Sodii Carbonas (U. S. P., 1890), but more so than Sodii Bicarbonas.

Solubility.—Soluble in water (1:2.9), in boiling water (1:1.8), in glycerin (1:8); insoluble in alcohol.

Dose.—"Average dose: 0.250 Gm. = 250 milligrammes (4 grains)." (U. S. P.)

SODII CITRAS.

Sodium Citrate.



Properties.—A white, granular powder, odorless. It slowly effloresces on exposure to dry air. Soluble in 1.1 parts of cold water and in 0.4 part of boiling water; slightly soluble in alcohol.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

A carbonated solution of Sodium Citrate is contained in the National Formulary under the name of Liquor Sodii Citratis and in the German Pharmacopœia under the name Potio Riveri.

SODII PHOSPHAS EFFERVESCENS.

Effervescent Sodium Phosphate.

A similar compound is official under the same name in the British Pharmacopœia.

It is composed of the Exsiccated Sodium Phosphate, Sodium Bicarbonate, and Tartaric and Citric acids. It contains just sufficient sodium bicarbonate to neutralize the tartaric and citric acids when it is dissolved in water, and the carbonic acid gas liberated gives a pleasant acidulous and effervescent taste.

Dose.—"Average dose: 8 Gm. (120 grains)." (U. S. P.)

It should be kept in well stoppered bottles.

SODII PHOSPHAS EXSICCATUS.

Exsiccated Sodium Phosphate.



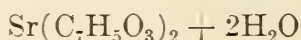
This is also called anhydrous sodium phosphate; it is obtained by driving off the water of crystallization of Sodium Phosphate (U. S. P.), which amounts to 60.3 per cent of the latter's weight. In a given weight of the exsiccated salt there are two and a half times as much sodium phosphate as in the same weight of the crystallized salt.

It is a white powder which absorbs moisture readily when exposed to the air and is gradually transformed into a salt of the composition $\text{Na}_2\text{HPO}_4 + 7\text{H}_2\text{O}$, which contains about 47 per cent of water; the latter salt is permanent.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

STRONTII SALICYLAS.

Strontium Salicylate.



Character.—White, crystalline powder, odorless and having a sweetish saline taste.

Solubility.—Soluble in water (1:18) and alcohol (1:66), much more so when these are boiling.

Incompatibility.—Incompatible with ferric salts, mineral acids, quinine salts in solution, spirit of nitrous ether, and sodium phosphate in powder.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

Keep in well stoppered bottles, protected from heat and light.

Strontium Lactate (U. S. P., 1890) has been dismissed from the Pharmacopœia; the bromide and iodide are retained.

STROPHANTHINUM.**Strophanthin.**

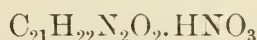
A glucoside or mixture of glucosides, obtained from *Strophanthus*.

Character.—A white or faintly yellowish crystalline powder, containing varying amounts of water of crystallization. Permanent in the air. Taste intensely bitter; great caution should be used in tasting it.

Solubility.—Very soluble in water and diluted alcohol.

Dose.—"Average dose: 0.0003 Gm.=0.3 milligramme ($\frac{1}{200}$ grain)." (U. S. P.)

Caution.—Keep in well stoppered amber colored bottles. Its solutions are very liable to decompose and should be freshly prepared. Exceedingly powerful poison. There is no known chemical assay for this drug and, as it is liable to variation, physicians would do well to secure specimens which have been tested physiologically.

STRYCHNINE NITRAS.**Strychnine Nitrate.**

Character.—Colorless, glistening needles, odorless, and having an intensely bitter taste; permanent in the air.

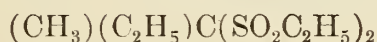
Solubility.—Soluble in water (1:42), alcohol (1:120), and glycerin (1:60); much more soluble in warm water or alcohol.

The hydrochloride (the only strychnine salt official in the Br. P.) and the Sulphate (already official in the U. S. P.) both contain water of crystallization and effloresce in dry air. The Nitrate (the only salt official in the P. G.) contains no water of crystallization and is permanent in the air.

Dose.—"Average dose: 0.001 Gm.=1 milligramme ($\frac{1}{64}$ grain)." (U. S. P.)

SULPHONETHYLMETHANUM.**Sulphonethylmethane.**

(*Trional*.)



This substance is commonly known by the trade name, *trional*. It is official in the German Pharmacopœia under the name Methylsulphonum; in the French and Swedish Pharmacopœias it is called Trional, and in the Austrian Pharmacopœia, Trionalum. It should not be confused with Sulphonmethanum (q. v.) (*sulphonal*).

Chemistry.—Chemically it is diethylsulphonemethylethylmethane ($\begin{pmatrix} \text{CH}_3 \\ \text{C}_2\text{H}_5 \end{pmatrix} > \text{C} < \begin{pmatrix} \text{SO}_2\text{C}_2\text{H}_5 \\ \text{SO}_2\text{C}_2\text{H}_5 \end{pmatrix}$) and may be regarded as methane (CH_4) in which two hydrogen atoms are replaced by ethylsulphone ($\text{SO}_2\text{C}_2\text{H}_5$)

groups, one by a methyl (CH_3) and the fourth by an ethyl (C_2H_5) group. (For method of preparation see Sulphonmethanum.)

Character.—"Colorless, lustrous, odorless, crystalline scales which have a bitter taste in aqueous solution."

Solubility.—"Soluble in 195 parts of water, more readily in boiling water, and readily soluble in alcohol and ether."

It melts at 76°C .; hence if a test-tube containing some of the powder be placed in hot water, the substance will melt; Sulphonmethanum (the melting point of which is 125.5°C .) will not melt under these circumstances.

The aqueous solution should be neutral to litmus paper; no odor should be evolved when 1 Gm. is dissolved in 50 Cc. of boiling water.

Dose.—"Average dose: 1 Gm. (15 grains)." (U. S. P.)

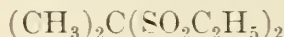
The German Pharmacopœia fixes 2 Gm. as the largest single dose and 4 Gm. as the maximum amount to be given in one day.

Caution.—Should not be combined in full dose with full doses of other drugs of similar physiological action, e. g., Hydrated Chloral, Chloralformamide, Sulphonmethane, etc.

SULPHONMETHANUM.

Sulphonmethane.

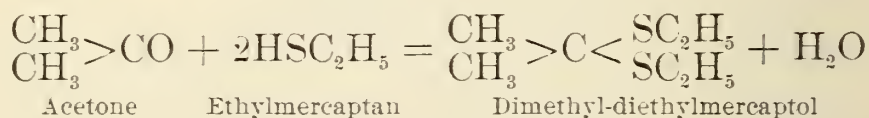
(*Sulphonal*.)



This substance is commonly known by the trade name, *sulphonal*—a name which has been adopted by the British and several other Pharmacopœias. It should not be confused with Sulphonethylmethanum (q. v.).

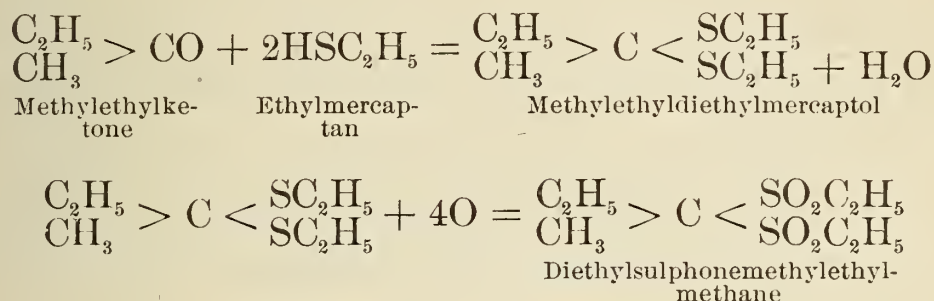
Chemistry.—Chemically it is diethylsulphonedimethylmethane

$\begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} > \text{C} < \begin{array}{c} \text{SO}_2\text{C}_2\text{H}_5 \\ \text{SO}_2\text{C}_2\text{H}_5 \end{array}$ The chemical structure of this substance, as well as that of Sulphonethylmethane, is explained by the following reactions involved in one process of its manufacture: acetone and ethylmercaptan unite (under the influence of dry hydrochloric acid gas) to form dimethyldiethylmercaptol



Through oxidation with potassium permanganate the sulphur atoms combine with oxygen to form sulphone (SO_2) groups; the resulting product is diethylsulphonedimethylmethane $(\text{CH}_3)_2\text{C}(\text{SO}_2\text{C}_2\text{H}_5)_2$ —a name shortened in the Pharmacopœia to Sulphonmethane. It may be regarded as methane (CH_4) in which two hydrogen atoms are replaced by methyl (CH_3) groups and two by ethylsulphone ($\text{SO}_2\text{C}_2\text{H}_5$) groups.

If methylethylketone $\begin{smallmatrix} \text{C}_2\text{H}_5 \\ \text{CH}_3 \end{smallmatrix} > \text{CO}$ be used in the above process instead of acetone, diethylsulphonemethylethylmethane (Sulphonethylmethanum, U. S. P.) is formed:



The chemical name is abbreviated by the Pharmacopœia to “Sulphonethylmethane” which is commonly known as *trional*; the *tri* of the latter name indicates the presence of three ethyl (C_2H_5) groups. If two ethyl groups are introduced in the place of the methyl groups, the resulting compound $\begin{smallmatrix} \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{smallmatrix} > \text{C} < \begin{smallmatrix} \text{SO}_2\text{C}_2\text{H}_5 \\ \text{SO}_2\text{C}_2\text{H}_5 \end{smallmatrix}$ is what is commonly known as *tetronal*; the latter name indicates the presence of four ethyl groups. As a general rule, the introduction of ethyl groups into a compound increases the hypnotic action.

Character.—Colorless, odorless, and nearly tasteless prismatic crystals, permanent in the air.

Solubility.—Soluble in water (1:360) and in alcohol (1:47), much more so in boiling water (1:15) and boiling alcohol (1:2). It melts at 125.5°C . A pure preparation is neutral to litmus and evolves no odor when boiled with water.

Dose.—“Average dose: 1 Gm. (15 grains).” (U. S. P.)

The German Pharmacopœia fixes the maximum single dose at 2 Gm.; the maximum daily dose at 4 Gm. Kast recommends that not more than 2 Gm. be given to a man nor more than 1 Gm. to a woman at a single dose, and that if the drug is used for any length of time the administration be frequently discontinued for from one to several days. The urine should be watched, and if there are indications of hæmaturia the use of the drug should be discontinued.

SYRUPUS HYPOPHOSPHITUM COMPOSITUS.

Compound Syrup of Hypophosphites.

Syrupus Hypophosphitum cum Ferro (U. S. P., 1890), is dropped, but this may take its place, as it contains iron (although in considerably smaller proportion). It contains 5 hypophosphites, Hypophosphorous Acid, Quinine, and Strychnine. It is adopted (with slight changes) from the National Formulary and is similar to a number of well-known commercial articles.

Dose.—“Average dose: 8 Cc. (2 fluidrachms).” (U. S. P.)

TALCUM.**Talc.**

A native hydrous magnesium silicate, official under the same name in the German Pharmacopœia. The German Pharmacopœia contains a dusting powder *Pulvis salicylicus cum Talco* consisting of salicylic acid, starch, and talc; some of the commercial talcum powders contain talc and boracic acid.

Properties.—Talc occurs as a grayish-green solid with waxy luster, or a white or pale gray powder. It feels greasy to the touch, hence it is popularly called soapstone. It is used as a dusting powder, and in some pill masses.

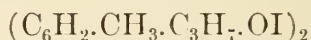
TALCUM PURIFICATUM.**Purified Talc.**

Talcum purified by treatment with hydrochloric acid. Used in the pharmacopœial method of preparing certain official waters of volatile oils.

The same preparation is to be found in the National Formulary.

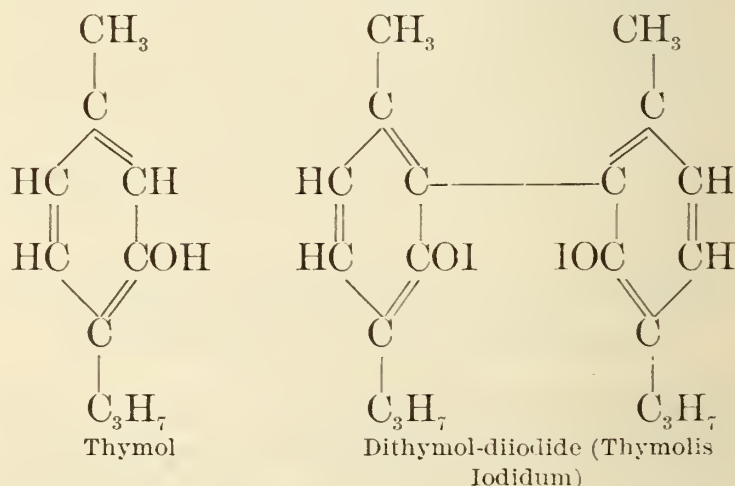
THYMOLIS IODIDUM.**Thymol Iodide.**

(*Aristol.*)



Official in the French Pharmacopœia as Diiodothymol. Various known as *aristol*, *annidalin*, and *thymotol*.

Chemistry.—Chemically it is dithymol-diiodide. It is obtained by the condensation of two molecules of thymol (a methylisopropylphenol) and the introduction into its phenolic group of two atoms of iodine:



Character.—A bright, chocolate-colored or reddish-yellow, bulky powder, almost tasteless, and having a slight aromatic odor.

Solubility.—Insoluble in water and glycerin, soluble with difficulty in alcohol, readily soluble in fatty oils and in ether, vaseline, chloroform, and collodion.

It contains 46.14 per cent of iodine (Iodoform contains 96.7 per cent, Iodol 89 per cent of iodine).

Caution.—Keep in amber-colored bottles, protected from light.

Other thymol derivatives.—Many other derivatives or compounds of thymol have been suggested for therapeutic use, e. g., *thymotal* (thymol-carbonate), *thymacetin* (analogous to *phenacetin*), *thymoform* (condensation product of thymol and formaldehyde), *iodothymoform* (iodized *thymoform*), mercury compounds of thymol, *thymosalol*, etc.

TINCTURA GAMBIR COMPOSITA.

Compound Tincture of Gambir.

To replace Tinctura Catechu Composita (U. S. P., 1890). (See Gambir.)

Dose.—“Average dose: 4 Cc. (1 fluidrachm).” (U. S. P.)

TINCTURA LIMONIS CORTICIS.

Tincture of Lemon Peel.

Similar to the Tinctura Limonis (Br. P.), but twice as strong.

TROCHISCI GAMBIR.

Troches of Gambir.

To replace Trochisci Catechu (U. S. P., 1890).

UNGUENTUM ACIDI BORICI.

Ointment of Boric Acid.

A 10 per cent ointment made with Paraffin and White Petrolatum. Similar to the Unguentum Acidi Borici of the British and German Pharmacopœias.

UNGUENTUM HYDRARGYRI DILUTUM.

Blue Ointment.

This preparation contains 67 per cent of Unguentum Hydrargyri, which is called Mercurial Ointment. Heretofore “Blue Ointment” and “Mercurial Ointment” have been synonymous. Mercurial Ointment contains about 50 per cent of metallic mercury, while Blue Ointment contains about 33.5 per cent.

UNGUENTUM ZINCI STEARATIS.

Ointment of Zinc Stearate.

An ointment containing 50 per cent of Zinc Stearate. The zinc present in the ointment is equivalent to about 7.5 or 8 per cent of zinc oxide.

VANILLINUM.

Vanillin.



Methyl ether of protocatechuic aldehyde $\text{C}_6\text{H}_3 \begin{array}{l} \nearrow \text{CHO (1)} \\ \text{--- OCH}_3 \text{ (3)} \\ \searrow \text{OH (4)} \end{array}$, occurring naturally in vanilla or made synthetically. Vanilla (U. S. P.) contains from 1 to 2 or 3 per cent of vanillin.

Eugenol, the principal constituent of oil of cloves, is allylmethyl pyrocatechol, and by oxidation yields vanillin, the allyl group being oxidized to the aldehyde group, (CHO), present in vanillin.

Character.—Colorless, prismatic needles, having the odor and taste of vanilla, and melting at 80° to 81° C.

Solubility.—Soluble in cold water (about 1:100), in warm (1:15), easily soluble in alcohol, glycerin, ether, and chloroform.

Being a phenol in character, it readily dissolves in dilute alkali hydroxides, from which it is precipitated by acids. It is extracted completely from its solution in ether by shaking with a saturated aqueous solution of sodium bisulphite, from which it may be precipitated again by sulphuric acid.

Purity.—The Pharmacopœia guards against a possible adulteration with acetanilide by the following test: on warming 0.1 Gm. of Vanillin with concentrated alcoholic solution of sodium hydroxide, adding chloroform and again warming it should not give the disgusting odor of phenyl isocyanide; such an odor would indicate acetanilide.

Dose.—"Average dose: 0.030 Gm.=30 milligrammes ($\frac{1}{2}$ grain)." (U. S. P.)

Caution.—Keep in well-stoppered bottles, in a cool place, and protected from the light.

Coumarin $\left(\text{C}_6\text{H}_4 \begin{array}{l} \nearrow \text{O-CO} \\ \text{---} \\ \searrow \text{CH=CH} \end{array} \right)$ the anhydride of orthocinnamic acid

is an odoriferous principle found in the Tonka bean (1.5 per cent), and elsewhere, which resembles vanillin in odor. It forms colorless, shining prisms, melting at 67° C., and soluble in 400 parts cold, 45 parts of hot water, and in 7.5 parts of alcohol, easily soluble in ether.

"Extracts of vanilla" are sometimes found to be made not from the true vanilla bean, but to be alcoholic tinctures of synthetic vanillin or coumarin. Such sophistication can readily be detected, as follows: If some of the extract be freed from alcohol by evaporation, made up to its original volume with water and acidified with acetic acid, a reddish brown precipitate of resin will form in the case of a true extract; absence of such resin would indicate an artificial extract. The filtrate from this resin, in a true extract, should give a copious precipitate with basic lead acetate solution; an artificial gives none.

Distinction between vanillin and coumarin: an aqueous solution of vanillin is turned blue by a few drops of ferric chloride solution (U. S. P. test), coumarin is not. An aqueous solution of coumarin, unlike vanillin, forms a precipitate, when iodine in potassium iodide is added in excess, at first brown and flocculent, and afterwards, on shaking, forming a dark-green curdy clot.

A case has recently been reported in which vanillin was adulterated (to the extent of 50 per cent) with terpin hydrate; the adulteration was readily detected by the lack of a definite melting point.

VINUM COCÆ.

Wine of Coca.

An official wine prepared from the Fluidextract of Coca; it may well replace some of the commercial articles of this name.

Dose.—"Average dose: 16 Cc. (4 fluidrachms)." (U. S. P.)

This is practically the same preparation as the Vinum Erythroxyli, N. F.

ZINCI PHENOLSULPHONAS.

Zinc Phenolsulphonate.



Commonly known as zinc sulphocarbolate; official in British Pharmacopœia as Zinci Sulphocarbolas. It should contain not less than 99.5 per cent of pure zinc paraphenolsulphonate. $(\text{C}_6\text{H}_4(\text{OH})\text{SO}_3)_2\text{Zn}$ 1:4+8H₂O.

Character.—Colorless, transparent, rhombic prisms, or tabular crystals, odorless, and having an astringent, metallic taste; effloresces on exposure and may become pink.

Solubility.—Easily soluble in water or alcohol. The aqueous solution is acid to litmus.

Dose.—"Average dose: 0.125 Gm.=125 milligrammes (2 grains)." (U. S. P.)

Caution.—Keep in small, well-stoppered bottles.

ZINCI STEARAS.

Zinc Stearate.

Used in preparing Unguentum Zinci Stearatis.

CHANGES IN STRENGTH OF THE MORE IMPORTANT OFFICIAL PREPARATIONS.

(a) *Table of More Important Pharmacopœial Preparations, the Strength of which has been Increased.*

TITLE.	CHIEF CONSTITUENT.	PHARMACOPŒIA, 1890.	EIGHTH DECENNIAL REVISION.
Acidum Sulphuricum Aromaticum	H ₂ SO ₄ , by weight.....	About 18.5 per cent.....	About 20.0 per cent.
Alcohol	Absolute Alcohol, by weight.....	About 91.0 per cent.....	About 92.3 per cent.
Alcohol Dilutum	Absolute Alcohol, by weight.....	About 41.0 per cent.....	About 41.5 per cent.
Caffeina Citrata Effervescens.....	Citrated Caffeine, by weight.....	2.0 Gm. in 100 Gm.....	4.0 Gm. in 100 Gm.
Extractum Opii	Morphine (cryst.), by weight.....	18.0 per cent.....	20.0 per cent.
Liquor Ferri et Ammonii Acetatis.....	Tincture of Ferric Chloride.....	2 Cc. in 100 Cc.....	4 Cc. in 100 Cc.
Liquor Ferri Tersulphatis.....	Fe ₂ (SO ₄) ₃ , by weight.....	28.7 per cent.....	36.0 per cent.
Manganii Dioxidum Precipitatum ^a	Manganese Dioxide.....	At least 65.0 per cent.....	At least 80.0 per cent.
Oleatum Hydrargyri	Yellow Mercuric Oxide, by weight.....	20.0 per cent.....	25.0 per cent.
Tinctura Aurantii Dulcis.....	Sweet Orange Peel.....	1 Gm. in 5.0 Cc.....	1 Gm. in 2.0 Cc.
Tinctura Calumbæ	Calumba.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Tinctura Cantharidis.....	Cantharides.....	1 Gm. in 20.0 Cc.....	1 Gm. in 10.0 Cc.
Tinctura Capsici.....	Capsicum.....	1 Gm. in 20.0 Cc.....	1 Gm. in 10.0 Cc.
Tinctura Cardamomi.....	Cardamom.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Tinctura Cinnamomi.....	Saigon Cinnamon.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Tinctura Quassie.....	Quassia.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Tinctura Rhei.....	Rhubarb.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Tinctura Serpentarie	Serpentaria.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Tinctura Strophanthi	Strophanthus.....	1 Gm. in 20.0 Cc.....	1 Gm. in 10.0 Cc.
Tinctura Tolutana	Balsam of Tolu.....	1 Gm. in 10.0 Cc.....	1 Gm. in 5.0 Cc.
Unguentum Chrysarobini.....	Chrysarobin, by weight.....	About 5.0 per cent.....	About 6.0 per cent.
Vinum Ergotæ	Fluidextract Ergot.....	1 Gm. in 6.67 Cc.....	1 Cc. Fluidextract Ergot in 5 Cc.

^a See page 46.

(b) Table of More Important Pharmacopœial Preparations, the Strength of which has been Decreased.

TITLE.	CHIEF CONSTITUENT.	PHARMACOPŒIA, 1890.	EIGHTH DECENNIAL REVISION.
Calx Chlorinata	Available Cl, by weight.....	At least 35.0 per cent	At least 30.0 per cent.
Jalap	{ Alcohol-soluble resin, by weight.....	12.0 per cent.....	At least 8.0 per cent.
Liquor Ferri Chloridi	{ Ether-soluble resin, by weight	Not more than 1.2 per cent.....	Not more than 1.5 per cent.
Lithii Citras Effervescens	Anhydrous FeCl ₃ , by weight.....	37.8 per cent.....	29.0 per cent.
Opil Pulvis	Lithium Citrate, by weight.....	About 17.0 per cent.....	About 5.0 per cent.
Opium Deodoratum	Morphine (cryst.), by weight	13 to 15 per cent	12 to 12.5 per cent.
Potassii Citras Effervescens	Morphine (cryst.), by weight	13 to 15 per cent	12 to 12.5 per cent.
Spiritus Frumenti	Potassium Citrate, by weight	About 48.0 per cent.....	About 20.0 per cent.
Suppositoria Glycerini	Absolute Alcohol, by weight.....	44 to 50 per cent	37 to 47.5 per cent.
Syrupus Ferri Iodidi	Glycerin, (half their former size)	6 Gm. each	3 Gm. each.
Tinctura Aconiti	Ferrous Iodide, by weight.....	About 10 per cent.....	About 5 per cent.
Tinctura Belladonnæ Foliorum	Aconite	1 Gm. in 2.85 Ce	1 Gm. in 10.0 Ce.
Tinctura Benzoini Composita	Belladonna Leaves.....	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Cannabis Indicæ	Benzoin	1 Gm. in 8.33 Ce	1 Gm. in 10.0 Ce.
Tinctura Colehici Seminis	Indian Cannabis	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Digitalis	Colechicum Seed	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Ferri Chloridi	Digitalis.....	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Gambir Composita ^a	Anhydrous FeCl ₃ , by weight	13.6 per cent.....	13.28 per cent.
Tinctura Gelsenii	Gambir	1 Gm. in 10.0 Ce	1 Gm. in 20.0 Ce.
Tinctura Hyoseyami	Gelsemium	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Kino	Hyoseyamus.....	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Lobellæ	Kino	1 Gm. in 10.0 Ce	1 Gm. in 20.0 Ce.
Tinctura Opi	Lobelia.....	1 Gm. in 5.0 Ce	1 Gm. in 10.0 Ce.
Tinctura Opi Deodorata	Morphine (cryst.), by weight	1.3 to 1.5 Gm. in 100 Ce	1.2 to 1.25 Gm. in 100 Ce.
Tinctura Physostigmatis	Morphine (cryst.), by weight	1.3 to 1.5 Gm. in 100 Ce	1.2 to 1.25 Gm. in 100 Ce.
Tinctura Sanguinarie	Physostigma	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Scillæ	Sanguinaria	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
Tinctura Stramonii	Squill	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.
	Stramonium.....	1 Gm. in 6.67 Ce	1 Gm. in 10.0 Ce.

^a See Gambir, p. 37.

(b) *Table of More Important Pharmacopœial Preparations, the Strength of which has been Decreased—Continued.*

TITLE.	CHIEF CONSTITUENT.	PHARMACOPŒIA, 1890.	EIGHTH DECENNIAL REVISION.
Tinctura Veratri	Veratrum	1 Gm. in 2.5 Cc	1 Gm. in 10.0 Cc.
Trochisci Cubebe	Oleoresin of Cubebe, by weight	0.01 Gm. in each	0.02 Gm in each.
Unguentum Phenolis	Phenol, by weight	About 5.0 per cent.	About 3.0 per cent.
Unguentum Sulphuris	Washed Sulphur, by weight	About 30.0 per cent.	About 15.0 per cent.
Vinum Album	Absolute Alcohol, by weight	10.0 to 14.0 per cent.	7.0 to 12.0 per cent.
Vinum Colechici Seminis	Fluidextract Colechicum Seed	1 Gm. Colechicum Seed in 6.67 Cc	1 Cc. Fluidextract Colechicum Seed in 10.0 Cc.
Vinum Rubrum	Absolute Alcohol, by weight	10.0 to 14.0 per cent.	7.0 to 12.0 per cent.

(c) *Table of More Important Pharmacopœial Preparations, for which a Standard has been Fixed, or made More Definite.*

TITLE.	CHIEF CONSTITUENT.	PHARMACOPŒIA, 1890.	EIGHTH DECENNIAL REVISION.
Aconitum	Aconitine, by weight.....	Standard not fixed	At least 0.5 per cent.
Belladonnæ Folia	Mydriatic alkaloids, by weight.....	Standard not fixed	At least 0.35 per cent.
Belladonnæ Radix	Mydriatic alkaloids, by weight.....	Standard not fixed	At least 0.5 per cent.
Cinchona.....	Alkaloids, by weight.....	At least 2.5 per cent Quinine.....	At least 4 per cent ether-soluble alkaloids.
Coca.....	Ether-soluble alkaloids, by weight.....	Standard not fixed	At least 0.5 per cent.
Colchici Cormus.....	Colchicine, by weight.....	Standard not fixed	At least 0.35 per cent.
Colchici Semen.....	Colchicine, by weight.....	Standard not fixed	At least 0.55 per cent.
Conium.....	Coniine, by weight.....	Standard not fixed	At least 0.5 per cent.
Emplastrum Belladonnæ.....	Mydriatic alkaloids, by weight.....	Standard not fixed	Not less than 0.38 per cent nor more than 0.42 per cent.
Extractum Belladonnæ.....	Mydriatic alkaloids, by weight.....	Standard not fixed	1.4 per cent.
Extractum Colchici Cormi.....	Colchicine, by weight.....	Standard not fixed	1.4 per cent.
Extractum Hyoscyami.....	Mydriatic alkaloids, by weight.....	Standard not fixed	0.3 per cent.
Extractum Nuclei Vomice.....	Strychnine, by weight.....	15.0 per cent total alkaloids.....	5.0 per cent.
Extractum Physostigmatis.....	Ether-soluble alkaloids, by weight.....	Standard not fixed	2.0 per cent.
Extractum Stramonii.....	Mydriatic alkaloids, by weight.....	Standard not fixed	1.4 per cent.
Fluidextractum Aconiti.....	Aconitine, by weight.....	Standard not fixed	0.4 Gm. in 100 Cc.
Fluidextractum Belladonnæ Radicis.....	Mydriatic alkaloids, by weight.....	Standard not fixed	0.5 Gm. in 100 Cc.
Fluidextractum Cinchonæ.....	Anhydrous ether-soluble alkaloids, by weight.....	Standard not fixed	4.0 Gm. in 100 Cc.
Fluidextractum Cocæ.....	Ether-soluble alkaloids, by weight.....	Standard not fixed	0.5 Gm. in 100 Cc.
Fluidextractum Colchici Seminis.....	Colchicine, by weight.....	Standard not fixed	0.5 Gm. in 100 Cc.
Fluidextractum Conii.....	Coniine, by weight.....	Standard not fixed	0.45 Gm. in 100 Cc.
Fluidextractum Guaranæ.....	Alkaloids, by weight.....	Standard not fixed	3.5 Gm. in 100 Cc.
Fluidextractum Hydrastis.....	Hydrastine, by weight.....	Standard not fixed	2.0 Gm. in 100 Cc.
Fluidextractum Hyoscyami.....	Mydriatic alkaloids, by weight.....	Standard not fixed	0.075 Gm. in 100 Cc.
Fluidextractum Ipecacuanhæ.....	Alkaloids, by weight.....	Standard not fixed	1.75 Gm. in 100 Cc.
Fluidextractum Nuclei Vomice.....	Strychnine, by weight.....	1.5 Gm. total alkaloids in 100 Cc.....	1.0 Gm. in 100 Cc.
Fluidextractum Pilocarpi.....	Alkaloids, by weight.....	Standard not fixed	0.4 Gm. in 100 Cc.
Fluidextractum Stramonii.....	Mydriatic alkaloids, by weight.....	Standard not fixed	0.35 Gm. in 100 Cc.

(c) *Table of More Important Pharmacopœial Preparations, for which a Standard has been Fixed, etc.—Continued.*

TITLE.	CHIEF CONSTITUENT.	PHARMACOPŒIA, 1890.	EIGHTH DECENNIAL REVISION.
Guarana.....	Alkaloids, by weight.....	Standard not fixed.....	At least 3.5 per cent.
Hydrastis.....	Hydrastine, by weight.....	Standard not fixed.....	At least 2.5 per cent.
Hyoscyamus.....	Mydriatic alkaloids, by weight.....	Standard not fixed.....	At least 0.08 per cent.
Ipecacuanha.....	Alkaloids, by weight.....	Standard not fixed.....	At least 2.0 per cent.
Jalap.....	{ Alcohol-soluble resin, by weight.....	12 per cent.....	At least 8.0 per cent.
Nux Vomica.....	{ Ether-soluble resin, by weight.....	Not more than 1.2 per cent.....	Not more than 1.5 per cent.
Oleum Amygdalæ Amare.....	Strychnine, by weight.....	Standard not fixed.....	At least 1.25 per cent.
Oleum Cajuputi.....	{ Benzaldehyde, by weight.....	Standard not fixed.....	At least 85.0 per cent.
Oleum Caryophylli.....	{ Hydrocyanic Acid, by weight.....	Standard not fixed.....	2 to 4 per cent.
Oleum Cinnamomi.....	Cincol, by volume.....	Standard not fixed.....	At least 55 per cent.
Oleum Eucalypti.....	Eugenol, by volume.....	Standard not fixed.....	At least 80 per cent.
Oleum Limonis.....	Cinnamic Aldehyde, by volume.....	Standard not fixed.....	At least 75 per cent.
Oleum Menthae Piperitæ.....	Cincol, by volume.....	Standard not fixed.....	At least 50 per cent.
Oleum Pimentæ.....	Citral, by weight.....	Standard not fixed.....	At least 4 per cent.
Oleum Rosmarini.....	{ Menthyl Acetate, by weight.....	Standard not fixed.....	At least 8 per cent.
Oleum Santali.....	{ Total Menthol, by weight.....	Standard not fixed.....	At least 50 per cent.
Oleum Thymi.....	Eugenol, by volume.....	Standard not fixed.....	At least 65 per cent.
Punereadum.....	{ Bornyl Acetate, by weight.....	Standard not fixed.....	At least 5 per cent.
	{ Total Bornicol, by weight.....	Standard not fixed.....	At least 15 per cent.
	Santalol, by weight.....	Standard not fixed.....	At least 90 per cent.
	Phenols, by volume.....	Standard not fixed.....	At least 20 per cent.
		Standard not fixed.....	1 part digests at least 25 parts of starch.
Physostigma.....	Ether-soluble alkaloids, by weight.....	Standard not fixed.....	At least 0.15 per cent.
Pilocarpus.....	Alkaloids, by weight.....	Standard not fixed.....	At least 0.5 per cent.
Stramonium.....	Mydriatic alkaloids, by weight.....	Standard not fixed.....	At least 0.35 per cent.
Tinctura Aconiti.....	Aconitine, by weight.....	Standard not fixed.....	0.045 Gm. in 100 Cc.
Tinctura Belladonnæ Foliorum.....	Mydriatic alkaloids, by weight.....	Standard not fixed.....	0.035 Gm. in 100 Cc.
Tinctura Colchici Seminibus.....	Colchicine, by weight.....	Standard not fixed.....	0.05 Gm. in 100 Cc.
Tinctura Hydrastis.....	Hydrastine, by weight.....	Standard not fixed.....	0.4 Gm. in 100 Cc.
Tinctura Hyoscyami.....	Mydriatic alkaloids, by weight.....	Standard not fixed.....	0.007 Gm. in 100 Cc.
Tinctura Nucis Vomicae.....	Strychnine, by weight.....	Standard not fixed.....	0.1 Gm. Strychnine in 100 Cc.
Tinctura Physostigmatis.....	Ether-soluble alkaloids, by weight.....	Standard not fixed.....	0.014 Gm. in 100 Cc.

CHANGES IN OFFICIAL LATIN TITLES OF PHARMACOPŒIAL PREPARATIONS.

Pharmacopœia, 1890.	Pharmacopœia, Eighth Revision.
Acidum Arsenosum	Arseni Trioxidum.
Acidum Carbolicum	Phenol.
Acidum Chromicum	Chromii Trioxidum.
Aloe Barbadensis	Aloe.
Aloe Socotrina	Aloe.
Alumini Hydras	Alumini Hydroxidum.
Ammonii Valerianas	Ammonii Valeras.
Amyl Nitris	Amylis Nitris.
Apomorphinæ Hydrochloras	Apomorphinæ Hydrochloridum.
Aqua Chlorig	Liquor Chlorig Compositus.
Argenti Nitras Dilutus	Argenti Nitras Mitigatus.
Arnicae Flores	Arnica.
Calx Chlorata	Calx Chlorinata.
Chloral	Chloralum Hydratum.
Cocainæ Hydrochloras	Cocainæ Hydrochloridum.
Colchici Radix	Colchici Cormus.
Emplastrum Resinæ	Emplastrum Adhæsivum.
Extractum Aconiti Fluidum	Fluidextractum Aconiti.
Extractum Apocyni Fluidum	Fluidextractum Apocyni.
Extractum Aromaticum Fluidum	Fluidextractum Aromaticum.
Extractum Aurantii Amari	Fluidextractum Aurantii Amari.
Extractum Belladonnæ Foliorum Alcoholicum	Extractum Belladonnæ Foliorum.
Extractum Belladonnæ Radicis Fluidum	Fluidextractum Belladonnæ Radicis.
Extractum Buchu Fluidum	Fluidextractum Buchu.
Extractum Calami Fluidum	Fluidextractum Calami.
Extractum Calumbæ Fluidum	Fluidextractum Calumbæ.
Extractum Cannabis Indicæ Fluidum	Fluidextractum Cannabis Indicæ.
Extractum Capsici Fluidum	Fluidextractum Capsici.
Extractum Chimaphilæ Fluidum	Fluidextractum Chimaphilæ.
Extractum Chiratæ Fluidum	Fluidextractum Chiratæ.
Extractum Cimicifugæ Fluidum	Fluidextractum Cimicifugæ.
Extractum Cinchonæ Fluidum	Fluidextractum Cinchonæ.
Extractum Cocæ Fluidum	Fluidextractum Cocæ.
Extractum Colchici Radicis	Extractum Colchici Cormi.
Extractum Colchici Seminis Fluidum	Fluidextractum Colchici Seminis.
Extractum Conii Fluidum	Fluidextractum Conii.
Extractum Convallariæ Fluidum	Fluidextractum Convallariæ.
Extractum Cubebæ Fluidum	Fluidextractum Cubebæ.
Extractum Cypripedii Fluidum	Fluidextractum Cypripedii.
Extractum Digitalis Fluidum	Fluidextractum Digitalis.
Extractum Ergotæ Fluidum	Fluidextractum Ergotæ.
Extractum Eriodictyi Fluidum	Fluidextractum Eriodictyi.
Extractum Eucalypti Fluidum	Fluidextractum Eucalypti.
Extractum Eupatorii Fluidum	Fluidextractum Eupatorii.
Extractum Frangulæ Fluidum	Fluidextractum Frangulæ.
Extractum Gelsemii Fluidum	Fluidextractum Gelsemii.

Changes in official Latin titles of pharmacopœial preparations—Continued.

Pharmacopœia, 1890.	Pharmacopœia, Eighth Revision.
Extractum Gentianæ Fluidum.....	Fluidextractum Gentianæ.
Extractum Geranii Fluidum.....	Fluidextractum Geranii.
Extractum Glycyrrhizæ Fluidum.....	Fluidextractum Glycyrrhizæ.
Extractum Grindeliæ Fluidum.....	Fluidextractum Grindeliæ.
Extractum Guaranæ Fluidum.....	Fluidextractum Guaranæ.
Extractum Hamamelidis Fluidum.....	Fluidextractum Hamamelidis Foliorum.
Extractum Hydrastis Fluidum.....	Fluidextractum Hydrastis.
Extractum Hyoscyami Fluidum.....	Fluidextractum Hyoscyami.
Extractum Ipecacuanhæ Fluidum.....	Fluidextractum Ipecacuanhæ.
Extractum Kramerie Fluidum.....	Fluidextractum Kramerie.
Extractum Lappæ Fluidum.....	Fluidextractum Lappæ.
Extractum Leptandræ Fluidum.....	Fluidextractum Leptandræ.
Extractum Lobeliæ Fluidum.....	Fluidextractum Lobeliæ.
Extractum Lupulini Fluidum.....	Fluidextractum Lupulini.
Extractum Matico Fluidum.....	Fluidextractum Matico.
Extractum Mezerei Fluidum.....	Fluidextractum Mezerei.
Extractum Nucis Vomice Fluidum.....	Fluidextractum Nucis Vomice.
Extractum Pareiræ Fluidum.....	Fluidextractum Pareiræ.
Extractum Phytolacæ Radicis Fluidum.....	Fluidextractum Phytolacæ.
Extractum Pilocarpi Fluidum.....	Fluidextractum Pilocarpi.
Extractum Podophylli Fluidum.....	Fluidextractum Podophylli.
Extractum Pruni Virginianæ Fluidum.....	Fluidextractum Pruni Virginianæ.
Extractum Quassie Fluidum.....	Fluidextractum Quassie.
Extractum Rhamni Purshianæ Fluidum.....	Fluidextractum Rhamni Purshianæ.
Extractum Rhei Fluidum.....	Fluidextractum Rhei.
Extractum Rhois Glabræ Fluidum.....	Fluidextractum Rhois Glabræ.
Extractum Rosæ Fluidum.....	Fluidextractum Rosæ.
Extractum Rubi Fluidum.....	Fluidextractum Rubi.
Extractum Sabinæ Fluidum.....	Fluidextractum Sabinæ.
Extractum Sanguinariæ Fluidum.....	Fluidextractum Sanguinariæ.
Extractum Sarsaparillæ Fluidum.....	Fluidextractum Sarsaparillæ.
Extractum Sarsaparillæ Fluidum Compositum....	Fluidextractum Sarsaparillæ Compositum.
Extractum Scillæ Fluidum.....	Fluidextractum Scillæ.
Extractum Scutellariæ Fluidum.....	Fluidextractum Scutellariæ.
Extractum Senegæ Fluidum.....	Fluidextractum Senegæ.
Extractum Sennæ Fluidum.....	Fluidextractum Sennæ.
Extractum Serpentariæ Fluidum.....	Fluidextractum Serpentariæ.
Extractum Spigeliæ Fluidum.....	Fluidextractum Spigeliæ.
Extractum Stillingiæ Fluidum.....	Fluidextractum Stillingiæ.
Extractum Taraxaci Fluidum.....	Fluidextractum Taraxaci.
Extractum Tritici Fluidum.....	Fluidextractum Tritici.
Extractum Uvæ Ursi Fluidum.....	Fluidextractum Uvæ Ursi.
Extractum Valerianæ Fluidum.....	Fluidextractum Valerianæ.
Extractum Veratri Viridis Fluidum.....	Fluidextractum Veratri.
Extractum Viburni Opuli Fluidum.....	Fluidextractum Viburni Opuli.
Extractum Viburni Prunifolii Fluidum.....	Fluidextractum Viburni Prunifolii.
Extractum Xanthoxyli Fluidum.....	Fluidextractum Xanthoxyli.
Extractum Zingiberis Fluidum.....	Fluidextractum Zingiberis.
Ferri Oxidum Hydratum.....	Ferri Hydroxidum.
Ferri Oxidum Hydratum cum Magnesia.....	Ferri Hydroxidum cum Magnesii Oxido.
Glyceritum Acidi Carbolici.....	Glyceritum Phenolis.
Gossypii Radicis Cortex.....	Gossypii Cortex.
Guaiaci Resina.....	Guaiacum.
Hamamelis.....	Hamamelidis Folia.
Hydrastininæ Hydrochloras.....	Hydrastininæ Hydrochloridum.

Changes in official Latin titles of pharmacopœial preparations—Continued.

Pharmacopœia, 1890.	Pharmacopœia, Eighth Revision.
Hyoscinae Hydrobromas.....	Hyoscinae Hydrobromidum.
Hyoscyaminae Hydrobromas	Hyoscyaminae Hydrobromidum.
Liquor Potassæ.....	Liquor Potassii Hydroxidi.
Liquor Sodæ.....	Liquor Sodii Hydroxidi.
Liquor Sodæ Chloratæ	Liquor Sodæ Chlorinatæ.
Magnesia.....	Magnesi Oxidum.
Magnesia Ponderosa.....	Magnesi Oxidum Ponderosum.
Mangani Dioxidum	Mangani Dioxidum Præcipitatum.
Mel Despumatum	Mel Depuratum.
Methyl Salicylas	Methylis Salicylas.
Morphinae Hydrochloras	Morphinae Hydrochloridum.
Naphtalinum.....	Naphthalenum.
Naphtol	Betanaphthol.
Oleum Betulæ Volatile.....	Oleum Betulæ.
Petrolatum Molle	Petrolatum.
Petrolatum Spissum.....	Petrolatum.
Phytolaccæ Radix	Phytolacca.
Pilocarpinae Hydrochloras	Pilocarpinae Hydrochloridum.
Potassa	Potassii Hydroxidum.
Potassi Bichromas.....	Potassii Dichromas.
Quercus Alba.....	Quercus.
Quininae Hydrobromas.....	Quininae Hydrobromidum.
Quininae Hydrochloras.....	Quininae Hydrochloridum.
Resorcinum	Resorcinol.
Salol.....	Phenylis Salicylas.
Sevum.....	Sevum Preparatum.
Soda.....	Sodii Hydroxidum.
Sodii Hyposulphis.....	Sodii Thiosulphas.
Sodii Sulphocarbolas.....	Sodii Phenolsulphonas.
Spiritus Glonoini.....	Spiritus Glycerylis Nitratis.
Stramonii Folia	Stramonium.
Tinctura Arnicae Florum.....	Tinctura Arnicae.
Tinctura Stramonii Seminis.....	Tinctura Stramonii.
Tinctura Veratri Viridis.....	Tinctura Veratri.
Unguentum Acidi Carbolici.....	Unguentum Phenolis
Veratrum Viride	Veratrum.
Vinum Ferri Citratis	Vinum Ferri.
Zinci Valerianas.....	Zinci Valeras.

ARTICLES DISMISSED FROM THE PHARMACOPŒIA.

Absinthium.
Acidum Carbolicum Crudum.
Alcohol Deodoratum.¹
Allium.
Ammoniacum.
Ammonii Nitras.
Antimonii Oxidum.
Antimonii Sulphidum.
Antimonii Sulphidum Purificatum.
Antimonium Sulphuratum.
Argenti Iodidum.
Arnicae Radix.²
Asclepias.
Aspidosperma.
Barii Dioxidum.³
Bryonia.
Cascarilla.
Castanea.
Catechu.⁴
Caulophyllum.
Ceratum Cetacei.
Cetraria.
Charta Potassii Nitratis.
Chelidonium.
Chenopodium.
Cinchonina.⁵
Cinnamomum Cassia.⁶
Crocus.
Decoctum Cetrariæ.
Decoctum Sarsaparillæ Compositum.
Dulcamara.
Elixir Phosphori.⁷
Emplastrum Ammoniaci cum Hydrargyro.
Emplastrum Arnicae.
Emplastrum Ferri.
Emplastrum Ichthyocollæ.
Emplastrum Picis Burgundicæ.
Emplastrum Picis Cantharidatum.
Emplastrum Resinæ.⁸
Emulsum Ammoniaci.
Extractum Aconiti.⁹
Extractum Arnicae Radicis.
Extractum Arnicae Radicis Fluidum.
Extractum Asclepiadis Fluidum.
Extractum Aspidospermatis Fluidum.
Extractum Castaneæ Fluidum.
Extractum Cinchonæ.
Extractum Colchici Radicis Fluidum.¹⁰
Extractum Conii.
Extractum Cusso Fluidum.
Extractum Dulcamaræ Fluidum.
Extractum Gossypii Radicis Fluidum.¹¹
Extractum Iridis.
Extractum Iridis Fluidum.
Extractum Jalapæ.

Extractum Juglandis.
Extractum Lobeliæ Fluidum (hydro-alcoholic menstruum).¹²
Extractum Menispermii Fluidum.
Extractum Podophylli.
Extractum Rumicis Fluidum.
Extractum Sanguinariæ Fluidum (hydro-alcoholic menstruum).¹²
Extractum Scillæ Fluidum (hydro-alcoholic menstruum).¹²
Extractum Scoparii Fluidum.
Extractum Stramonii Seminis.¹³
Extractum Stramonii Seminis Fluidum.
Extractum Uvæ Ursi.
Ferri Iodidum Saccharatum.
Ferri Lactas.
Ferri Valerianas.
Glyceritum Vitelli.
Guaiaci Lignum.
Hydrargyri Cyanidum.
Hydrargyri Subsulphas Flavus.
Ichthyocolla.
Illicium.
Infusum Cinchonæ.
Inula.
Iris.
Juglans.
Kamala.
Linimentum Sinapis Compositum.
Liquor Ferri Acetatis.
Liquor Ferri Citratis.
Liquor Ferri Nitratis.
Liquor Sodii Silicatis.
Macis.
Magnesii Citras Effervescens.¹⁴
Massa Copaibæ.
Melissa.
Menispermum.
Oleatum Zinci.¹⁵
Oleum Aurantii Florum.¹⁶
Oleum Bergamottæ.
Oleum Myrciæ.
Oleum Phosphoratum.
Oleum Sesami.
Pepsinum Saccharatum.
Phytolacæ Fructus.¹⁷
Picrotoxinum.
Pilulæ Alæs et Asafœtidæ.
Pilulæ Antimonii Compositæ.
Pilulæ Rhei.
Pix Burgundica.
Plumbi Carbonas.
Potassa cum Calce.
Potassa Sulphurata.
Pulsatilla.

Pulvis Antimonialis.
 Quinidinæ Sulphas.
 Quininæ Valerianas.
 Resina Copaibæ.
 Rhus Toxicodendron.
 Rosa Centifolia.
 Rubus Idæus.
 Rumex.
 Sambucus.
 Sodii Carbonas.¹⁸
 Sodii Carbonas Exsiccat.¹⁸
 Spiritus Aurantii.
 Spiritus Limonis.¹⁹
 Spiritus Myrciæ.
 Spiritus Myristicæ.
 Spiritus Phosphori.
 Stramonii Semen.¹³
 Strontii Lactas.
 Syrupus Allii.
 Syrupus Althææ.
 Syrupus Hypophosphitum cum Ferro.²⁰
 Syrupus Rubi Idæi.
 Tabacum.
 Tanacetum.

Tinctura Arnicæ Radicis.
 Tinctura Bryoniæ.
 Tinctura Catechu Composita.²¹
 Tinctura Chirataë.
 Tinctura Croci.
 Tinctura Cubebæ.
 Tinctura Humuli.
 Tinctura Matico.
 Tinctura Rhei Dulcis.
 Tinctura Stramonii Seminis.¹³
 Tinctura Sumbul.²²
 Trochisci Catechu.²³
 Trochisci Cretæ.
 Trochisci Ferri.
 Trochisci Ipecacuanhæ.
 Trochisci Menthæ Piperitæ.
 Trochisci Morphinæ et Ipecacuanhæ.
 Trochisci Zingiberis.
 Unguentum Plumbi Carbonatis.
 Unguentum Plumbi Iodidi.
 Unguentum Stramonii (seed).²⁴
 Vinum Colchici Radicis.²⁵
 Vitellus.
 Zinci Phosphidum.

¹ The standard of Alcohol in the Eighth Revision has been raised, making it about equivalent to Alcohol Deodoratum (U. S. P., 1890).

² Arnicæ Flores (U. S. P., 1890) becomes Arnica in the present revision.

³ Never used in medicine; heretofore only in the preparation of Aqua Hydrogenii Dioxidii.

⁴ Replaced by Gambir.

⁵ Cinchoninæ Sulphas is retained.

⁶ Saigon and Ceylon are retained, and Cinnamic Aldehyde, the most important constituent of Cinamon, has been introduced.

⁷ The Pills of Phosphorus are retained.

⁸ Replaced by Emplastrum Adhæsivum.

⁹ Alkaloid Aconitine introduced.

¹⁰ Fluidextractum Colchici Seminis is retained, and Colchicine is introduced.

¹¹ Gossypii Radicis Cortex (1890) = Gossypii Cortex, Eighth Revision.

¹² The new Fluidextractum is a hydro-acetic acid extract.

¹³ Stramonii Folia (1890) = Stramonium, Eighth Revision, of which there are an extract, a fluid-extract and a tincture. The present extract is made from the fluidextract.

¹⁴ See Magnesii Sulphas Effervescens, page 45.

¹⁵ See Zinci Stearas, page 61.

¹⁶ Oleum Aurantii Corticis is retained.

¹⁷ Phytolaccæ Radix (1890) = Phytolacca, Eighth Revision.

¹⁸ See Sodii Carbonas Monohydratus, page 53.

¹⁹ Tinctura Limonis is introduced.

²⁰ See Syrupus Hypophosphitum Compositus, page 57.

²¹ Replaced by Tinctura Gambir Composita.

²² Fluidextractum Sumbul is introduced.

²³ Replaced by Trochisci Gambir.

²⁴ Made from Extractum Stramonii, Eighth Revision.

²⁵ Vinum Colchici Seminis is retained.

TABLE OF AVERAGE DOSES, AS GIVEN BY THE U. S. PHARMACOPŒIA, EIGHTH DECENNIAL REVISION.

The Pharmacopœial Convention of 1900 instructed the Committee of Revision “to state the average approximate (but neither a maximum nor a minimum) dose for adults, * * * the metric system to be used, and the approximate equivalent ordinary weights or measures inserted in parentheses,” and the Committee was further directed to make the following distinct declaration: “That neither this Convention, nor the Committee of Revision created by it, intends to have these doses regarded as obligatory on the physician or as forbidding him to exceed them whenever in his judgment this seems advisable.”

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision.

PREPARATION.	AVERAGE DOSE.	
	Metrie System.	Approximate Equivalent Ordinary System.
Acetamidum	0. 250 Gm. = 250 milligrammes.	4 grains.
Acetphenetidinum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Acetum Opii	0. 5 Cc.	8 minims.
Acetum Scillæ	1 Cc.	15 minims.
Acidum Aceticum Dilutum	2 Cc.	30 minims.
Acidum Benzoicum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Acidum Boricum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Acidum Camphoricum	1 Gm.	15 grains.
Acidum Citricum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Acidum Gallicum	1 Gm.	15 grains.
Acidum Hydriodicum Dilutum	0. 5 Cc.	8 minims.
Acidum Hydrobromicum Dilutum	4 Cc.	1 fluidrachm.
Acidum Hydrochloricum Dilutum	1 Cc.	15 minims.
Acidum Hydrocyanicum Dilutum	0. 1 Cc.	1½ minims.
Acidum Hypophosphorosum Dilutum	0. 5 Cc.	8 minims.
Acidum Lacticum	2 Cc.	30 minims.
Acidum Nitricum Dilutum	2 Cc.	30 minims.
Acidum Nitrohydrochloricum	0. 2 Cc.	3 minims.
Acidum Nitrohydrochloricum Dilutum	1 Cc.	15 minims.
Acidum Phosphoricum Dilutum	2 Cc.	30 minims.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Acidum Salicylicum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Acidum Sulphuricum Aromaticum	1 Cc.	15 minims.
Acidum Sulphuricum Dilutum	2 Cc.	30 minims.
Acidum Sulphurosum	2 Cc.	30 minims.
Acidum Tannicum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Acidum Tartaricum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Aconitina	0. 00015 Gm. = 0.15 milligramme.	$\frac{1}{400}$ grain.
Aconitum	0. 065 Gm. = 65 milligrammes.	1 grain.
Æther	1 Cc.	15 minims.
Æther Aceticus	1 Cc.	15 minims.
Æthylis Carbamas	1 Gm.	15 grains.
Aloe	0. 250 Gm. = 250 milligrammes.	4 grains.
Aloe Purificata	0. 250 Gm. = 250 milligrammes.	4 grains.
Aloinum	0. 065 Gm. = 65 milligrammes.	1 grain.
Alumen	0. 500 Gm. = 500 milligrammes.	7½ grains.
Ammonii Benzoas	1 Gm.	15 grains.
Ammonii Bromidum	1 Gm.	15 grains.
Ammonii Carbonas	0. 250 Gm. = 250 milligrammes.	4 grains.
Ammonii Chloridum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Ammonii Iodidum	0. 250 Gm. = 250 milligrammes.	4 grains.

Ammonii Salicylas	0. 250 Gm. = 250 milligrammes.	4 grains.
Ammonii Valeras	0. 500 Gm. = 500 milligrammes.	7½ grains.
Amylis Nitris	0. 2 Cc.	3 minims.
Anisum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Anthemis	2 Gm.	30 grains.
Antimonii et Potassii Tartas	0. 005 Gm. = 5 milligrammes.	⅙ grain.
Antipyrina	0. 030 Gm. = 30 milligrammes.	½ grain.
Apocynum	0. 250 Gm. = 250 milligrammes.	4 grains.
Apomorphine Hydrochloridum	1 Gm.	15 grains.
Apomorphine Hydrochloridum	0. 002 Gm. = 2 milligrammes.	⅙ grain.
Apomorphine Hydrochloridum	0. 005 Gm. = 5 milligrammes.	⅙ grain.
Aqua Ammoniac	1 Cc.	15 minims.
Aqua Amygdale Amare	4 Cc.	1 fluidrachm.
Aqua Anisi	16 Cc.	4 fluidrachms.
Aqua Aurantii Florum	16 Cc.	4 fluidrachms.
Aqua Aurantii Florum Fortior	8 Cc.	2 fluidrachms.
Aqua Camphoræ	8 Cc.	2 fluidrachms.
Aqua Chloroformi	16 Cc.	4 fluidrachms.
Aqua Cinnamomi	16 Cc.	4 fluidrachms.
Aqua Creosoti	8 Cc.	2 fluidrachms.
Aqua Fœniculi	16 Cc.	4 fluidrachms.
Aqua Hamamelidis	8 Cc.	2 fluidrachms.
Aqua Hydrogenii Dioxidii	4 Cc.	1 fluidrachm.
Aqua Menthæ Piperitæ	16 Cc.	4 fluidrachms.
Aqua Menthæ Viridis	16 Cc.	4 fluidrachms.
Aqua Rosæ	16 Cc.	4 fluidrachms.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Aqua Rose Fortior.....	8 Cc.	2 fluidrachms.
Argenti Nitras	0. 010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
Argenti Oxidum	0. 065 Gm. = 65 milligrammes.	1 grain.
Arnica	1 Gm.	15 grains.
Arseni Iodidum	0. 005 Gm. = 5 milligrammes.	$\frac{1}{16}$ grain.
Arseni Trioxidum	0. 002 Gm. = 2 milligrammes.	$\frac{1}{36}$ grain.
Asafetida	0. 250 Gm. = 250 milligrammes.	4 grains.
Aspidium	4 Gm.	60 grains.
Atropina	0. 0004 Gm. = 0. 4 milligramme.	$\frac{1}{160}$ grain.
Atropinæ Sulphas	0. 0004 Gm. = 0. 4 milligramme.	$\frac{1}{160}$ grain.
Aurantii Amari Cortex	1 Gm.	15 grains.
Aurantii Dulcis Cortex	1 Gm.	15 grains.
Auri et Sodii Chloridum	0. 005 Gm. = 5 milligrammes.	$\frac{1}{16}$ grain.
Balsamum Peruvianum	1 Gm.	15 grains.
Balsamum Tolutanum	1 Gm.	15 grains.
Belladonnæ Folia	0. 065 Gm. = 65 milligrammes.	1 grain.
Belladonnæ Radix	0. 045 Gm. = 45 milligrammes.	$\frac{3}{4}$ grain.
Benzaldehydum	0. 03 Cc.	$\frac{1}{2}$ minim.
Benzoinum	1 Gm. •	15 grains.
Benzosulphimidum	0. 200 Gm. = 200 milligrammes.	3 grains.

Berberis.....	2 Gm.	30 grains.
Betanaphthol.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Bismuthi Citras.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Bismuthi et Ammonii Citras.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Bismuthi Subcarbonas.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Bismuthi Subgallas.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Bismuthi Subnitras.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Bismuthi Subsalicylas.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Bromoformum.....	0. 2 Cc.	3 minims.
Buchu.....	2 Gm.	30 grains.
Caffeina.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Caffeina Citrata.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Caffeina Citrata Effervescens.....	4 Gm.	60 grains.
Calamus.....	1 Gm.	15 grains.
Calcii Bromidum.....	1 Gm.	15 grains.
Calcii Carbonas Precipitatus.....	1 Gm.	15 grains.
Calcii Chloridum.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Calcii Hypophosphis.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Calcii Phosphas Precipitatus.....	1 Gm.	15 grains.
Calendula.....	1 Gm.	15 grains.
Calumba.....	2 Gm.	30 grains.
Calx Chlorinata.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Calx Sulphurata.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Canbogia.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Camphora.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Camphora Monobromata.....	0. 125 Gm. = 125 milligrammes.	2 grains.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Cannabis Indica	0.065 Gm. = 65 milligrammes.	1 grain.
Cantharis	0.030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Capsicum	0.065 Gm. = 65 milligrammes.	1 grain.
Carbo Ligni	1 Gm.	15 grains.
Cardamomum	1 Gm.	15 grains.
Carum	1 Gm.	15 grains.
Caryophyllus	0.250 Gm. = 250 milligrammes.	4 grains.
Cassia Fistula	4 Gm.	60 grains.
Cerri Oxalas	0.065 Gm. = 65 milligrammes.	1 grain.
Chimaphila	2 Gm.	30 grains.
Chirata	1 Gm.	15 grains.
Chloralformamidum	1 Gm.	15 grains.
Chloralum Hydratum	1 Gm.	15 grains.
Chloroformum	0.3 Cc.	5 minims.
Chondrus	15 Gm.	4 drachms.
Chrysarobinum	0.030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Cimicifuga	1 Gm.	15 grains.
Cinchona	1 Gm.	15 grains.
Cinchona Rubra	1 Gm.	15 grains.
Cinchonidinæ Sulphas	0.250 Gm. = 250 milligrammes.	4 grains.

Cinchoninæ Sulphas.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Cinnaldehydum.....	0. 05 Cc.	1 minim.
Cinnamomum Saigonicum.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Cinnamomum Zeylanicum.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Coca.....	2 Gm.	30 grains.
Cocaina.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Cocainæ Hydrochloridum.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Codeina.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Codeinæ Phosphas.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Codeinæ Sulphas.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Colchici Cormus.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Colchici Semen.....	0. 200 Gm. = 200 milligrammes.	3 grains.
Colchicina.....	0. 0005 Gm. = 0.5 milligrammes.	$\frac{1}{128}$ grain.
Colocynthis.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Confectio Sennæ.....	4 Gm.	60 grains.
Conium.....	0. 200 Gm. = 200 milligrammes.	3 grains.
Convallaria.....	0. 500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Copaiba.....	1 Cc.	15 minims.
Coriandrum.....	0. 500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Creosotum.....	0. 2 Cc.	3 minims.
Cresol.....	0. 05 Cc.	1 minim.
Creta Præparata.....	1 Gm.	15 grains.
Cubeba.....	1 Gm.	15 grains.
Cupri Sulphas.....	0. 010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
	0. 250 Gm. = 250 milligrammes.	4 grains.
Cusso.....	16 Gm.	240 grains.

{ Astringent.
 { Emetic

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Cypripedium	1 Gm.	15 grains.
Digitalis	0.065 Gm. = 65 milligrammes.	1 grain.
Elatérinum	0.005 Gm. = 5 milligrammes.	$\frac{1}{16}$ grain.
Elixir Ferri, Quininae, et Strychninae Phosphatum	4 Cc.	1 fluidrachm.
Emulsum Amygdalæ	120 Cc.	4 fluidounces.
Emulsum Asafoetida	16 Cc.	4 fluidrachms.
Emulsum Chloroformi	8 Cc.	2 fluidrachms.
Emulsum Olei Morrhuae	8 Cc.	2 fluidrachms.
Emulsum Olei Morrhuae cum Hypophosphitibus	8 Cc.	2 fluidrachms.
Emulsum Olei Terebinthinae	4 Cc.	1 fluidrachm.
Ergota.....	2 Gm.	30 grains.
Eriodictyon.....	1 Gm.	15 grains.
Eucalyptol.....	0.3 Cc.	5 minims.
Eucalyptus	2 Gm.	30 grains.
Eugenol	0.2 Cc.	3 minims.
Euonymus.....	0.500 Gm. = 500 milligrammes.	7½ grains.
Eupatorium.....	2 Gm.	30 grains.
Extractum Aloes.....	0.125 Gm. = 125 milligrammes.	2 grains.
Extractum Belladonnae Foliorum	0.010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
Extractum Cannabis Indicae	0.010 Gm. = 10 milligrammes	$\frac{1}{3}$ grain.

Extractum Cimicifugæ.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Colchici Corni.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Extractum Colocythidis.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Extractum Colocynthis Compositum.....	0. 500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Extractum Digitalis.....	0. 010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
Extractum Ergotæ.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Euonymi.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Extractum Gentianæ.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Glycyrrhizæ.....	1 Gm.	15 grains.
Extractum Glycyrrhizæ Purum.....	1 Gm.	15 grains.
Extractum Hæmatoxyli.....	1 Gm.	15 grains.
Extractum Hyoscyami.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Extractum Kramerizæ.....	0. 500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Extractum Leptandrz.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Malti.....	16 Cc.	4 fluidrachms.
Extractum Nucis Vomice.....	0. 015 Gm. = 15 milligrammes.	$\frac{1}{4}$ grain.
Extractum Opii.....	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Extractum Physostigmatis.....	0. 008 Gm. = 8 milligrammes.	$\frac{1}{8}$ grain.
Extractum Quassizæ.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Extractum Rhamni Purshianæ.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Rhei.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Scopulæ.....	0. 010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
Extractum Stramonii.....	0. 010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
Extractum Sumbul.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Extractum Taraxaci.....	1 Gm.	15 grains.
Fel Bovis Purificatum.....	0. 500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Ferri Carbonas Saccharatus	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri Chloridum	0.065 Gm. = 65 milligrammes.	1 grain.
Ferri Citras	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri et Ammonii Citras	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri et Ammonii Sulphas	0.500 Gm. = 500 milligrammes.	7½ grains.
Ferri et Ammonii Tartras	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri et Potassii Tartras	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri et Quininae Citras	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri et Quininae Citras Solubilis	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri et Strychninae Citras	0.125 Gm. = 125 milligrammes.	2 grains.
Ferri Hydroxidum cum Magnesii Oxido	120 Cc.	4 fluidounces.
Ferri Hypophosphis	0.200 Gm. = 200 milligrammes.	3 grains.
Ferri Phosphas Solubilis	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri Pyrophosphas Solubilis	0.250 Gm. = 250 milligrammes.	4 grains.
Ferri Sulphas	0.200 Gm. = 200 milligrammes.	3 grains.
Ferri Sulphas Exsiccatus	0.125 Gm. = 125 milligrammes.	2 grains.
Ferri Sulphas Granulatus	0.200 Gm. = 200 milligrammes.	3 grains.
Ferrum Reductum	0.065 Gm. = 65 milligrammes.	1 grain.
Fluidextractum Aconiti	0.05 Cc.	1 minim.
Fluidextractum Apocyni	1 Cc.	15 minims.

Fluidextractum Aromaticum.....	1 Cc.	15 minims.
Fluidextractum Aurantii Amari.....	1 Cc.	15 minims.
Fluidextractum Belladonnæ Radicis.....	0.05 Cc.	1 minim.
Fluidextractum Berberidis.....	2 Cc.	30 minims.
Fluidextractum Buchu.....	2 Cc.	30 minims.
Fluidextractum Calami.....	1 Cc.	15 minims.
Fluidextractum Calumbæ.....	2 Cc.	30 minims.
Fluidextractum Cannabis Indicæ.....	0.05 Cc.	1 minim.
Fluidextractum Capsici.....	0.05 Cc.	1 minim.
Fluidextractum Chinaphile.....	2 Cc.	30 minims.
Fluidextractum Chiratæ.....	1 Cc.	15 minims.
Fluidextractum Cimicifugæ.....	1 Cc.	15 minims.
Fluidextractum Cinchonæ.....	1 Cc.	15 minims.
Fluidextractum Cocce.....	2 Cc.	30 minims.
Fluidextractum Colechici Seminis.....	0.2 Cc.	3 minims.
Fluidextractum Conii.....	0.2 Cc.	3 minims.
Fluidextractum Convallariæ.....	0.5 Cc.	8 minims.
Fluidextractum Cubebæ.....	1 Cc.	15 minims.
Fluidextractum Cypripedii.....	1 Cc.	15 minims.
Fluidextractum Digitalis.....	0.05 Cc.	1 minim.
Fluidextractum Ergotæ.....	2 Cc.	30 minims.
Fluidextractum Eriodictyi.....	1 Cc.	15 minims.
Fluidextractum Eucalypti.....	2 Cc.	30 minims.
Fluidextractum Euonymi.....	0.5 Cc.	8 minims.
Fluidextractum Eupatorii.....	2 Cc.	30 minims.
Fluidextractum Frangulæ.....	1 Cc.	15 minims.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Fluidextractum Gelsenii	0.05 Cc.	1 minim.
Fluidextractum Gentianæ	1 Cc.	15 minims.
Fluidextractum Geranii	1 Cc.	15 minims.
Fluidextractum Glycyrrhizæ	2 Cc.	30 minims.
Fluidextractum Granati	2 Cc.	30 minims.
Fluidextractum Grindeliæ	2 Cc.	30 minims.
Fluidextractum Guaranzæ	2 Cc.	30 minims.
Fluidextractum Hamamelidis Foliorum	2 Cc.	30 minims.
Fluidextractum Hydrastis	2 Cc.	30 minims.
Fluidextractum Hyoscyami	0.2 Cc.	3 minims.
Fluidextractum Ipecacuanhæ	1 Cc.	15 minims.
	0.05 Cc.	1 minim.
Fluidextractum Kramerizæ	1 Cc.	15 minims.
Fluidextractum Lappæ	2 Cc.	30 minims.
Fluidextractum Leptandrzæ	1 Cc.	15 minims.
Fluidextractum Lobeliæ	0.5 Cc.	8 minims.
Fluidextractum Lupulini	0.5 Cc.	8 minims.
Fluidextractum Matico	4 Cc.	1 fluidrachm.
Fluidextractum Nucis Vomizæ	0.05 Cc.	1 minim.
Fluidextractum Pareiræ	2 Cc.	30 minims.

Fluidextractum Phytolacæ.....			15 minims.
Fluidextractum Pilocarpi.....	1 Cc.		1½ minims.
Fluidextractum Podophylli.....	0.1 Cc.		30 minims.
Fluidextractum Pruni Virginianæ.....	2 Cc.		8 minims.
Fluidextractum Quassie.....	0.5 Cc.		30 minims.
Fluidextractum Quercus.....	2 Cc.		8 minims.
Fluidextractum Quillajæ.....	0.5 Cc.		15 minims.
Fluidextractum Rhamni Purshianæ.....	1 Cc.		3 minims.
Fluidextractum Rhamni Purshianæ Aromaticum.....	0.2 Cc.		15 minims.
Fluidextractum Rhei.....	1 Cc.		15 minims.
Fluidextractum Rhois Glabræ.....	1 Cc.		15 minims.
Fluidextractum Rose.....	1 Cc.		15 minims.
Fluidextractum Rubi.....	2 Cc.		30 minims.
Fluidextractum Sabinae.....	1 Cc.		15 minims.
Fluidextractum Sanguinariæ.....	0.3 Cc.		5 minims.
Fluidextractum Sarsaparillæ.....	0.1 Cc.		1½ minims.
Fluidextractum Sarsaparillæ Compositum.....	2 Cc.		30 minims.
Fluidextractum Scillæ.....	2 Cc.		30 minims.
Fluidextractum Scopolæ.....	0.1 Cc.		1½ minims.
Fluidextractum Scutellariæ.....	0.05 Cc.		1 minim.
Fluidextractum Senegæ.....	1 Cc.		15 minims.
Fluidextractum Sennæ.....	1 Cc.		15 minims.
Fluidextractum Serpentariæ.....	2 Cc.		30 minims.
Fluidextractum Spigeliæ.....	1 Cc.		15 minims.
Fluidextractum Staphisagriæ.....	4 Cc.		1 fluidrachm.
	0.05 Cc.		1 minim.

{ Emetic ----
Alterative..

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Fluidextractum Stillingie.....	2 Cc.	30 minims.
Fluidextractum Stramonii.....	0.05 Cc.	1 minim.
Fluidextractum Sumbul.....	2 Cc.	30 minims.
Fluidextractum Taraxaci.....	8 Cc.	2 fluidrachms.
Fluidextractum Tritici.....	8 Cc.	2 fluidrachms.
Fluidextractum Uvæ Ursi.....	2 Cc.	30 minims.
Fluidextractum Valeriane.....	2 Cc.	30 minims.
Fluidextractum Veratri.....	0.1 Cc.	1½ minims.
Fluidextractum Viburni Opuli.....	2 Cc.	30 minims.
Fluidextractum Viburni Prunifolii.....	2 Cc.	30 minims.
Fluidextractum Xanthoxyli.....	2 Cc.	30 minims.
Fluidextractum Zingiberis.....	1 Cc.	15 minims.
Fœniculum.....	1 Gm.	15 grains.
Frangula.....	1 Gm.	15 grains.
Galla.....	0.500 Gm. = 500 milligrammes.	7½ grains.
Gambir.....	1 Gm.	15 grains.
Gelsemium.....	0.065 Gm. = 65 milligrammes.	1 grain.
Gentiana.....	1 Gm.	15 grains.
Geranium.....	1 Gm.	15 grains.
Glandulæ Suprarenales Siccæ.....	0.250 Gm. = 250 milligrammes.	4 grains.

Glandulæ Thyroidæ Siccæ	0. 250 Gm. = 250 milligrammes.	4 grains.
Glycerinum	4 Cc.	1 fluidrachm.
Glyceritum Acidi Tannici	2 Cc.	30 minims.
Glyceritum Ferri, Quininæ, et Strychinæ Phosphatum	1 Cc.	15 minims.
Glyceritum Hydrastis	2 Cc.	30 minims.
Glyceritum Phenolis	0. 3 Cc.	5 minims.
Glycyrrhiza	2 Gm.	30 grains.
Glycyrrhizinum Ammoniatum	0. 250 Gm. = 250 milligrammes.	4 grains.
Gossypii Cortex	2 Gm.	30 grains.
Granatum	2 Gm.	30 grains.
Grindelia	2 Gm.	30 grains.
Guaiacol	0. 5 Cc.	8 minims.
Guaiacolis Carbonas	1 Gm.	15 grains.
Guaiacum	1 Gm.	15 grains.
Guarana	2 Gm.	30 grains.
Hamamelidis Cortex	2 Gm.	30 grains.
Hamamelidis Folia	2 Gm.	30 grains.
Hedeoma	8 Gm.	120 grains.
Hexamethylenamina	0. 250 Gm. = 250 milligrammes.	4 grains.
Homatropinæ Hydrobromidum	0. 0005 Gm. = 0. 5 milligramme.	$\frac{1}{128}$ grain.
Humulus	2 Gm.	30 grains.
Hydrargyri Chloridum Corrosivum	0. 003 Gm. = 3 milligrammes.	$\frac{1}{20}$ grain.
Hydrargyri Chloridum Mite	0. 125 Gm. = 125 milligrammes.	2 grains.
Hydrargyri Iodidum Flavum	0. 065 Gm. = 65 milligrammes.	1 grain.
Hydrargyri Iodidum Rubrum	0. 010 Gm. = 10 milligrammes.	$\frac{1}{3}$ grain.
	0. 003 Gm. = 3 milligrammes.	$\frac{1}{20}$ grain.

{ Laxative
 } Alterative

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	Approximate Equivalent Ordinary System.
	Metric System.	
Hydargyrum cum Creta.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Hydrastina	0. 010 Gm. = 10 milligrammes.	$\frac{1}{5}$ grain.
Hydrastinae Hydrochloridum	0. 030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Hydrastis.....	2 Gm.	30 grains.
Hyoscinæ Hydrobromidum.....	0. 0005 Gm. = 0. 5 milligramme.	$\frac{1}{128}$ grain.
Hyoscyaminæ Hydrobromidum.....	0. 0005 Gm. = 0. 5 milligramme.	$\frac{1}{128}$ grain.
Hyoscyaminæ Sulphas	0. 0005 Gm. = 0. 5 milligramme.	$\frac{1}{128}$ grain.
Hyoscyamus.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Infusum Digitalis	8 Cc.	2 fluidrachms.
Infusum Pruni Virginianæ.....	60 Cc.	2 fluidounces.
Infusum Sennæ Compositum.....	120 Cc.	4 fluidounces.
Iodoformum	0. 250 Gm. = 250 milligrammes.	4 grains.
Iodolum	0. 250 Gm. = 250 milligrammes.	4 grains.
Iodum	0. 005 Gm. = 5 milligrammes.	$\frac{1}{16}$ grain.
Ipecacuanha	0. 065 Gm. = 65 milligrammes.	1 grain.
	1 Gm.	15 grains.
Jalapa.....	1 Gm.	15 grains.
Kino	0. 500 Gm. = 500 milligrammes.	7½ grains.
Krameria.....	1 Gm.	15 grains.
Lactucarium	1 Gm.	15 grains.

Lappa	2 Gm.	30 grains.
Leptandra	1 Gm.	15 grains.
Limonis Succus	30 Cc.	1 fluidounce.
Liquor Acidi Arsenosi	0.2 Cc.	3 minims.
Liquor Ammonii Acetatis	16 Cc.	4 fluidrachms.
Liquor Antisepticus	4 Cc.	1 fluidrachm.
Liquor Arseni et Hydrargyri Iodidi	0.1 Cc.	1½ minims.
Liquor Calcis	16 Cc.	4 fluidrachms.
Liquor Chlori Compositus	4 Cc.	1 fluidrachm.
Liquor Ferri Chloridi	0.1 Cc.	1½ minims.
Liquor Ferri et Ammonii Acetatis	16 Cc.	4 fluidrachms.
Liquor Ferri Subsulphatis	0.2 Cc.	3 minims.
Liquor Iodi Compositus	0.2 Cc.	3 minims.
Liquor Magnesii Citratis	360 Cc.	12 fluidounces.
Liquor Potassii Arsenitis	0.2 Cc.	3 minims.
Liquor Potassii Citratis	16 Cc.	4 fluidrachms.
Liquor Potassii Hydroxidi	1 Cc.	15 minims.
Liquor Sodæ Chlorinatæ	1 Cc.	15 minims.
Liquor Sodii Arsenatis	0.2 Cc.	3 minims.
Liquor Sodii Hydroxidi	1 Cc.	15 minims.
Liquor Sodii Phosphatis Compositus	8 Cc.	2 fluidrachms.
Lithii Benzoas	1 Gm.	15 grains.
Lithii Bromidum	1 Gm.	15 grains.
Lithii Carbonas	0.500 Gm. = 500 milligrammes.	7½ grains.
Lithii Citras	0.500 Gm. = 500 milligrammes.	7½ grains.
Lithii Citras Effervescens	8 Gm.	120 grains.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Lithii Salicylas	1 Gm.	15 grains.
Lobelia	0. 500 Gm. = 500 milligrammes.	7½ grains.
Lupulinum	0. 500 Gm. = 500 milligrammes.	7½ grains.
Magnesiæ Carbonas	3 Gm.	45 grains.
Magnesiæ Oxidum	2 Gm.	30 grains.
Magnesiæ Oxidum Ponderosum	2 Gm.	30 grains.
Magnesiæ Sulphas	16 Gm.	240 grains.
Magnesiæ Sulphas Effervescens	16 Gm.	240 grains.
Manganæ Dioxidum Precipitatum	0. 250 Gm. = 250 milligrammes.	4 grains.
Manganæ Hypophosphis	0. 200 Gm. = 200 milligrammes.	3 grains.
Manganæ Sulphas	0. 250 Gm. = 250 milligrammes.	4 grains.
Manna	16 Gm.	240 grains.
Marrubium	2 Gm.	30 grains.
Massa Ferri Carbonatis	0. 250 Gm. = 250 milligrammes.	4 grains.
Massa Hydrargyri	0. 250 Gm. = 250 milligrammes.	4 grains.
Mastiche	2 Gm.	30 grains.
Matico	4 Gm.	60 grains.
Matricaria	16 Gm.	240 grains.
Mel	4 Cc.	1 fluidrachm.
Mel Depuratum	4 Cc.	1 fluidrachm.

Mel Rose.....	4 Cc.	1 fluidrachm.
Mentha Piperita.....	4 Gm.	60 grains.
Mentha Viridis.....	4 Gm.	60 grains.
Menthol.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Methylis Salicylas.....	1 Cc.	15 minims.
Methylthionine Hydrochloridum.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Mezereum.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Mistura Cretæ.....	16 Cc.	4 fluidrachms.
Mistura Ferri Composita.....	16 Cc.	4 fluidrachms.
Mistura Glycyrrhizæ Composita.....	8 Cc.	2 fluidrachms.
Mistura Rhei et Sodæ.....	4 Cc.	1 fluidrachm.
Morphina.....	0. 010 Gm. = 10 milligrammes.	½ grain.
Morphinæ Acetas.....	0. 015 Gm. = 15 milligrammes.	¼ grain.
Morphinæ Hydrochloridum.....	0. 015 Gm. = 15 milligrammes.	¼ grain.
Morphinæ Sulphas.....	0. 015 Gm. = 15 milligrammes.	¼ grain.
Moschus.....	0. 250 Gm. = 250 milligrammes.	4 grains.
Mucilago Acaciæ.....	16 Cc.	4 fluidrachms.
Mucilago Sassafras Medullæ.....	16 Cc.	4 fluidrachms.
Mucilago Tragacanthæ.....	16 Cc.	4 fluidrachms.
Mucilago Ulmi.....	16 Cc.	4 fluidrachms.
Myristica.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Myrrha.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Naphthalenum.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Nux Vomica.....	0. 065 Gm. = 65 milligrammes.	1 grain.
Oleoresina Aspidii.....	2 Gm.	30 grains.
Oleoresina Capsici.....	0. 030 Gm. = 30 milligrammes.	½ grain.

Table of average doses, as given by the U. S. Pharmacopeia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Oleoresina Cubeæ	0.500 Gm. = 500 milligrammes.	7½ grains.
Oleoresina Lupulini	0.200 Gm. = 200 milligrammes.	3 grains.
Oleoresina Piperis	0.030 Gm. = 30 milligrammes.	½ grain.
Oleoresina Zingiberis	0.030 Gm. = 30 milligrammes.	½ grain.
Oleum Amygdalæ Amare	0.03 Cc.	½ minim.
Oleum Amygdalæ Expressum	30 Cc.	1 fluidounce.
Oleum Anisi	0.2 Cc.	3 minims.
Oleum Aurantii Corticis	0.2 Cc.	3 minims.
Oleum Betulæ	1 Cc.	15 minims.
Oleum Cajuputi	0.5 Cc.	8 minims.
Oleum Cari	0.2 Cc.	3 minims.
Oleum Caryophylli	0.2 Cc.	3 minims.
Oleum Chenopodii	0.2 Cc.	3 minims.
Oleum Cinnamomi	0.05 Cc.	1 minim.
Oleum Copaibæ	0.5 Cc.	8 minims.
Oleum Coriandri	0.2 Cc.	3 minims.
Oleum Cubeæ	0.5 Cc.	8 minims.
Oleum Erigerontis	1 Cc.	15 minims.
Oleum Eucalypti	0.5 Cc.	8 minims.
Oleum Fœniculi	0.2 Cc.	3 minims.

Oleum Gaultheriæ	1 Cc.	15 minims.
Oleum Gossypii Seminis	16 Cc.	4 fluidrachms.
Oleum Hedecmæ	0.2 Cc.	3 minims.
Oleum Juniperi	0.2 Cc.	3 minims.
Oleum Lavandulæ Florum	0.2 Cc.	3 minims.
Oleum Limonis	0.2 Cc.	3 minims.
Oleum Linî	30 Cc.	1 fluidounce.
Oleum Menthæ Piperitæ	0.2 Cc.	3 minims.
Oleum Menthæ Viridis	0.2 Cc.	3 minims.
Oleum Morrhuæ	16 Cc.	4 fluidrachms.
Oleum Myristicæ	0.2 Cc.	3 minims.
Oleum Olivæ	30 Cc.	1 fluidounce.
Oleum Picis Liquidæ	0.2 Cc.	3 minims.
Oleum Pimentæ	0.2 Cc.	3 minims.
Oleum Ricini	16 Cc.	4 fluidrachms.
Oleum Rosmarini	0.2 Cc.	3 minims.
Oleum Sabinæ	0.05 Cc.	1 minim.
Oleum Santali	0.5 Cc.	8 minims.
Oleum Sassafras	0.2 Cc.	3 minims.
Oleum Sinapis Volatile	0.008 Cc.	$\frac{1}{8}$ minim.
Oleum Terebinthinæ Rectificatum	1 Cc.	15 minims.
Oleum Thymî	0.2 Cc.	3 minims.
Oleum Tiglii	0.05 Cc.	1 minim.
Opî Pulvis	0.065 Gm. = 65 milligrammes.	1 grain.
Opium	0.100 Gm. = 100 milligrammes.	$1\frac{1}{2}$ grains.
Opium Deodoratum	0.065 Gm. = 65 milligrammes.	1 grain.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Opium Granulatum	0.065 Gm. = 65 milligrammes.	1 grain.
Pancreatinum	0.500 Gm. = 500 milligrammes.	7½ grains.
Paraldehydum	2 Cc.	30 minims.
Pareira	2 Gm.	30 grains.
Pelletierinæ Tannas	0.250 Gm. = 250 milligrammes.	4 grains.
Pepo	30 Gm.	1 ounce.
Pepsinum	0.250 Gm. = 250 milligrammes.	4 grains.
Phenol	0.065 Gm. = 65 milligrammes.	1 grain.
Phenol Liquefactum	0.05 Cc.	1 minim.
Phenylis Salicylas	0.500 Gm. = 500 milligrammes.	7½ grains.
Phosphorus	0.0005 Gm. = 0.5 milligramme.	1½⁄₈ grain.
Physostigma	0.100 Gm. = 100 milligrammes.	1½ grains.
Physostigminae Salicylas	0.001 Gm. = 1 milligramme.	1⁄₆₄ grain.
Physostigminae Sulphas	0.001 Gm. = 1 milligramme.	1⁄₆₄ grain.
Phytolacca	1 Gm.	15 grains.
Pilocarpinae Hydrochloridum	0.125 Gm. = 125 milligrammes.	2 grains.
Pilocarpinae Nitras	0.010 Gm. = 10 milligrammes.	1⁄₃ grain.
Pilocarpus	0.010 Gm. = 10 milligrammes.	1⁄₃ grain.
Pilulæ Aloes	2 Gm.	30 grains.
		2 pills.

Pilulæ Aloes et Ferri	2 pills.		
Pilulæ Aloes et Mastiches	2 pills.		
Pilulæ Aloes et Myrrhæ	2 pills.		
Pilulæ Asafoetidæ	2 pills.		
Pilulæ Cathartice Compositæ	2 pills.		
Pilulæ Cathartice Vegetabiles	2 pills.		
Pilulæ Ferri Carbonatis	2 pills.		
Pilulæ Ferri Iodidi	2 pills.		
Pilulæ Laxativæ Compositæ	2 pills.		
Pilulæ Opii	1 pill.		
Pilulæ Phosphori	1 pill.		
Pilulæ Podophylli, Belladonnæ et Capsici	1 pill.		
Pilulæ Rhei Compositæ	2 pills.		
Pimenta	1 Gm.	15 grains.	
Piper	0. 500 Gm. = 500 milligrammes.	7½ grains.	
Piperina	0. 200 Gm. = 200 milligrammes.	3 grains.	
Pix Liquida	0. 500 Gm. = 500 milligrammes.	7½ grains.	
Plumbi Acetas	0. 065 Gm. = 65 milligrammes.	1 grain.	
Podophyllum	0. 500 Gm. = 500 milligrammes.	7½ grains.	
Potassii Acetas	2 Gm.	30 grains.	
Potassii Bicarbonas	2 Gm.	30 grains.	
Potassii Bitartras	2 Gm.	30 grains.	
Potassii Bromidum	1 Gm.	15 grains.	
Potassii Carbonas	1 Gm.	15 grains.	
Potassii Chloras	0. 250 Gm. = 250 milligrammes.	4 grains.	
Potassii Citras	1 Gm.	15 grains.	

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Potassii Citras Effervescens	4 Gm.	60 grains.
Potassii Cyanidum	0.010 Gm. = 10 milligrammes.	$\frac{1}{5}$ grain.
Potassii Dichromas	0.010 Gm. = 10 milligrammes.	$\frac{1}{5}$ grain.
Potassii et Sodii Tartras	8 Gm.	120 grains.
Potassii Ferrocyanidum	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Potassii Hypophosphis	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Potassii Iodidum	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Potassii Nitras	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Potassii Pernanguanas	0.065 Gm. = 65 milligrammes.	1 grain.
Potassii Sulphas	2 Gm.	30 grains.
Prunus Virginiana	2 Gm.	30 grains.
Pulvis Acetanilidi Compositus	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Pulvis Aromaticus	1 Gm.	15 grains.
Pulvis Cretæ Compositus	2 Gm.	30 grains.
Pulvis Effervescens Compositus	1 set of two powders.	
Pulvis Glycyrrhizæ Compositus		
Pulvis Ipecacuanhæ et Opii	4 Gm.	60 grains.
Pulvis Jalapæ Compositus	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
Pulvis Morphinæ Compositus	2 Gm.	30 grains.
Pulvis Rhei Compositus	0.500 Gm. = 500 milligrammes.	$7\frac{1}{2}$ grains.
	2 Gm.	30 grains.

Pyrethrum	2 Gm.	30 grains.
Quassia.....	0. 500 Gm. = 500 milligrammes.	7½ grains.
Quercus	1 Gm.	15 grains.
Quinina	0. 250 Gm. = 250 milligrammes.	4 grains.
Quininae Bisulphas	0. 250 Gm. = 250 milligrammes.	4 grains.
Quininae Hydrobromidum	0. 250 Gm. = 250 milligrammes.	4 grains.
Quininae Hydrochloridum	0. 250 Gm. = 250 milligrammes.	4 grains.
Quininae Salicylas	0. 250 Gm. = 250 milligrammes.	4 grains.
Quininae Sulphas	0. 250 Gm. = 250 milligrammes.	4 grains.
Resina	0. 250 Gm. = 250 milligrammes.	4 grains.
Resina Jalapæ	0. 125 Gm. = 125 milligrammes.	2 grains.
Resina Podophylli	0. 015 Gm. = 15 milligrammes.	¼ grain.
Resina Scammonii.....	0. 005 Gm. = 5 milligrammes.	⅙ grain.
Resorcinol	0. 200 Gm. = 200 milligrammes.	3 grains.
Rhamnus Purshiana.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Rheum.....	1 Gm.	15 grains.
Rhus Glabra.....	1 Gm.	15 grains.
Rubus.....	1 Gm.	15 grains.
Sabal.....	1 Gm.	15 grains.
Sabina	0. 500 Gm. = 500 milligrammes.	7½ grains.
Safrolum	0. 3 Cc.	5 minims.
Salicinum	1 Gm.	15 grains.
Salvia	2 Gm.	30 grains.
Sanguinaria.....	0. 125 Gm. = 125 milligrammes.	2 grains.
Santoninum	0. 065 Gm. = 65 milligrammes.	1 grain.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Sarsaparilla.....	2 Gm.	30 grains.
Sassafras.....	8 Gm.	120 grains.
Scammonium.....	0.250 Gm. = 250 milligrammes.	4 grains.
Scilla.....	0.125 Gm. = 125 milligrammes.	2 grains.
Scoparius.....	.1 Gm.	15 grains.
Scopola.....	0.045 Gm. = 45 milligrammes.	$\frac{3}{4}$ grain.
Scopolamine Hydrobromidum.....	0.0005 Gm. = 0.5 milligramme.	$\frac{1}{128}$ grain.
Scutellaria.....	1 Gm.	15 grains.
Senega.....	1 Gm.	15 grains.
Senna.....	4 Gm.	60 grains.
Serpentaria.....	1 Gm.	15 grains.
Serum Antidiphthericum.....	{ Immunizing dose for well persons..	3,000 units.
Sinapis Alba.....		500 units.
Sinapis Nigra.....	8 Gm.	120 grains.
Sodii Acetas.....	8 Gm.	120 grains.
Sodii Arsenas.....	1 Gm.	15 grains.
Sodii Arsenas Exsiccatus.....	0.005 Gm. = 5 milligrammes.	$\frac{1}{16}$ grain.
Sodii Benzoas.....	0.003 Gm. = 3 milligrammes.	$\frac{1}{26}$ grain.
Sodii Bicarbonas.....	1 Gm.	15 grains.

Sodii Bisulphis.....	0.500 Gm. = 500 milligrammes.	7½ grains.
Sodii Boras.....	0.500 Gm. = 500 milligrammes.	7½ grains.
Sodii Bromidum.....	1 Gm.	15 grains.
Sodii Carbonas Monohydratus.....	0.250 Gm. = 250 milligrammes.	4 grains.
Sodii Chloras.....	0.250 Gm. = 250 milligrammes.	4 grains.
Sodii Chloridum.....	16 Gm.	240 grains.
Sodii Citras.....	1 Gm.	15 grains.
Sodii Hypophosphis.....	1 Gm.	15 grains.
Sodii Iodidum.....	0.500 Gm. = 500 milligrammes.	7½ grains.
Sodii Nitras.....	1 Gm.	15 grains.
Sodii Nitris.....	0.065 Gm. = 65 milligrammes.	1 grain.
Sodii Phenolsulphonas.....	0.250 Gm. = 250 milligrammes.	4 grains.
Sodii Phosphas.....	2 Gm.	30 grains.
Sodii Phosphas Effervescens.....	8 Gm.	120 grains.
Sodii Phosphas Exsiccatus.....	1 Gm.	15 grains.
Sodii Pyrophosphas.....	2 Gm.	30 grains.
Sodii Salicylas.....	1 Gm.	15 grains.
Sodii Sulphas.....	16 Gm.	240 grains.
Sodii Sulphis.....	1 Gm.	15 grains.
Sodii Thiosulphas.....	1 Gm.	15 grains.
Sparteine Sulphas.....	0.010 Gm. = 10 milligrammes.	⅓ grain.
Spigelia.....	4 Gm.	60 grains.
Spiritus Ætheris.....	4 Cc.	1 fluidrachm.
Spiritus Ætheris Compositus.....	4 Cc.	1 fluidrachm.
Spiritus Ætheris Nitrosi.....	2 Cc.	30 minims.
Spiritus Ammoniae.....	1 Cc.	15 minims.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Spiritus Ammoniac Aromaticus.....	2 Cc.	30 minims.
Spiritus Amygdalæ Amare	0.5 Cc.	8 minims.
Spiritus Anisi	4 Cc.	1 fluidrachm.
Spiritus Camphoræ.....	1 Cc.	15 minims.
Spiritus Chloroformi	2 Cc.	30 minims.
Spiritus Cinnamomi	2 Cc.	30 minims.
Spiritus Gaultheriæ.....	2 Cc.	30 minims.
Spiritus Glycerylis Nitratis.....	0.05 Cc.	1 minim.
Spiritus Juniperi	2 Cc.	30 minims.
Spiritus Juniperi Compositus.....	8 Cc.	2 fluidrachms.
Spiritus Lavandulæ	2 Cc.	30 minims.
Spiritus Menthæ Piperitæ.....	2 Cc.	30 minims.
Spiritus Menthæ Viridis	2 Cc.	30 minims.
Staphisagria	0.065 Gm. = 65 milligrammes.	1 grain.
Stillingia	2 Gm.	30 grains.
Stramonium	0.065 Gm. = 65 milligrammes.	1 grain.
Strontii Bromidum	1 Gm.	15 grains.
Strontii Iodidum	0.500 Gm. = 500 milligrammes.	7½ grains.
Strontii Salicylas.....	1 Gm.	15 grains.
Strophanthinum	0.0003 Gm. = 0.3 milligramme.	$\frac{1}{200}$ grain.

Strophanthus	0.065 Gm. = 65 milligrammes.	1 grain.
Strychnina	0.001 Gm. = 1 milligramme.	$\frac{1}{64}$ grain.
Strychninæ Nitras	0.001 Gm. = 1 milligramme.	$\frac{1}{64}$ grain.
Strychninæ Sulphas	0.001 Gm. = 1 milligramme.	$\frac{1}{64}$ grain.
Styrax	1 Gm.	15 grains.
Sulphonethylmethanum	1 Gm.	15 grains.
Sulphonmethanum	1 Gm.	15 grains.
Sulphur Lotum	4 Gm.	60 grains.
Sulphur Precipitatum	4 Gm.	60 grains.
Sulphur Sublimatum	4 Gm.	60 grains.
Sumbul	2 Gm.	30 grains.
Syrupus Acidi Hydriodici	4 Cc.	1 fluidrachm.
Syrupus Amygdalæ	4 Cc.	1 fluidrachm.
Syrupus Calcii Lactophosphatis	8 Cc.	2 fluidrachms.
Syrupus Calcis	2 Cc.	30 minims.
Syrupus Ferri Iodidi	1 Cc.	15 minims.
Syrupus Ferri, Quininae et Strychninae Phosphatum	4 Cc.	1 fluidrachm.
Syrupus Hypophosphitum	8 Cc.	2 fluidrachms.
Syrupus Hypophosphitum Compositus	8 Cc.	2 fluidrachms.
Syrupus Ipecacuanhæ	1 Cc.	15 minims.
	15 Cc.	4 fluidrachms.
Syrupus Krameriaë	4 Cc.	1 fluidrachm.
Syrupus Lactucarii	8 Cc.	2 fluidrachms.
Syrupus Picis Liquidæ	4 Cc.	1 fluidrachm.
Syrupus Pruni Virginianæ	4 Cc.	1 fluidrachm.
Syrupus Rhei	8 Cc.	2 fluidrachms.

{ Expectorant
Emetic

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Syrupus Rhei Aromaticus.....	8 Cc.	2 fluidrachms.
Syrupus Rubi.....	4 Cc.	1 fluidrachm.
Syrupus Sarsaparillæ Compositus.....	16 Cc.	4 fluidrachms.
Syrupus Scillæ.....	2 Cc.	30 minims.
Syrupus Scillæ Compositus.....	2 Cc.	30 minims.
Syrupus Senegæ.....	4 Cc.	1 fluidrachm.
Syrupus Sennæ.....	4 Cc.	1 fluidrachm.
Syrupus Tolutanus.....	16 Cc.	4 fluidrachms.
Syrupus Zingiberis.....	16 Cc.	4 fluidrachms.
Tamarindus.....	16 Gm.	240 grains.
Taraxacum.....	8 Gm.	120 grains.
Terebinum.....	0.5 Cc.	8 minims.
Terpini Hydras.....	0.125 Gm. = 125 milligrammes.	2 grains.
Thymol.....	0.125 Gm. = 125 milligrammes.	2 grains.
Tinctura Aconiti.....	0.6 Cc.	10 minims.
Tinctura Aloes.....	2 Cc.	30 minims.
Tinctura Aloes et Myrrhæ.....	2 Cc.	30 minims.
Tinctura Arnicæ.....	1 Cc.	15 minims.
Tinctura Asafoetide.....	1 Cc.	15 minims.
Tinctura Aurantii Amari.....	4 Cc.	1 fluidrachm.

Tinctura Aurantii Dulcis.....	4 Cc.	1 fluidrachm.
Tinctura Belladonnæ Foliorum.....	0.5 Cc.	8 minims.
Tinctura Benzoini.....	1 Cc.	15 minims.
Tinctura Benzoini Composita.....	2 Cc.	30 minims.
Tinctura Calumbæ.....	4 Cc.	1 fluidrachm.
Tinctura Cannabis Indicæ.....	0.6 Cc.	10 minims.
Tinctura Cantharidis.....	0.3 Cc.	5 minims.
Tinctura Capsici.....	0.5 Cc.	8 minims.
Tinctura Cardamomi.....	4 Cc.	1 fluidrachm.
Tinctura Cardamomi Composita.....	4 Cc.	1 fluidrachm.
Tinctura Cimicifugæ.....	4 Cc.	1 fluidrachm.
Tinctura Cinchonæ.....	4 Cc.	1 fluidrachm.
Tinctura Cinchonæ Composita.....	4 Cc.	1 fluidrachm.
Tinctura Cinnamomi.....	2 Cc.	30 minims.
Tinctura Colchici Seminis.....	2 Cc.	30 minims.
Tinctura Digitalis.....	1 Cc.	15 minims.
Tinctura Ferri Chloridi.....	0.5 Cc.	8 minims.
Tinctura Gallæ.....	4 Cc.	1 fluidrachm.
Tinctura Gambir Composita.....	4 Cc.	1 fluidrachm.
Tinctura Gelsemii.....	0.5 Cc.	8 minims.
Tinctura Gentianæ Composita.....	4 Cc.	1 fluidrachm.
Tinctura Guaiaci.....	4 Cc.	1 fluidrachm.
Tinctura Guaiaci Ammoniata.....	2 Cc.	30 minims.
Tinctura Hydrastis.....	4 Cc.	1 fluidrachm.
Tinctura Hyoscyami.....	1 Cc.	15 minims.
Tinctura Iodi.....	0.1 Cc.	1½ minims.

Table of average doses, as given by the U. S. Pharmacopœia, Eighth Decennial Revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Tinctura Ipecacuanhæ et Opii	0.5 Cc.	8 minims.
Tinctura Kino	4 Cc.	1 fluidrachm.
Tinctura Kramerie	4 Cc.	1 fluidrachm.
Tinctura Lactucarii	2 Cc.	30 minims.
Tinctura Lavandulæ Composita	2 Cc.	30 minims.
Tinctura Lobeliæ	1 Cc.	15 minims.
{ Expectorant.		1 fluidrachm.
{ Emetic.		1 fluidrachm.
Tinctura Moschi	4 Cc.	15 minims.
Tinctura Myrrhæ	1 Cc.	10 minims.
Tinctura Nucis Vomice	0.6 Cc.	8 minims.
Tinctura Opii	0.5 Cc.	2 fluidrachms.
Tinctura Opii Camphorata	8 Cc.	8 minims.
Tinctura Opii Deodorati	0.5 Cc.	15 minims.
Tinctura Physostigmatis	1 Cc.	30 minims.
Tinctura Quassie	2 Cc.	1 fluidrachm.
Tinctura Rhei	4 Cc.	30 minims.
Tinctura Rhei Aromatica	2 Cc.	15 minims.
Tinctura Sanguinariæ	1 Cc.	15 minims.
Tinctura Scille	1 Cc.	1 fluidrachm.
Tinctura Serpentariæ	4 Cc.	

Tinctura Stramonii	0.5 Cc.	8 minims.
Tinctura Strophanthi	0.5 Cc.	8 minims.
Tinctura Tolutana	2 Cc.	30 minims.
Tinctura Valerianæ	4 Cc.	1 fluidrachm.
Tinctura Valerianæ Ammoniata	2 Cc.	30 minims.
Tinctura Veratri	1 Cc.	15 minims.
Tinctura Zingiberis	2 Cc.	30 minims.
Triticum	8 Gm.	120 grains.
Trituratio Flaterini	0.030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Uva Ursi	2 Gm.	30 grains.
Valeriana	2 Gm.	30 grains.
Vanilla	1 Gm.	15 grains.
Vanillinum	0.030 Gm. = 30 milligrammes.	$\frac{1}{2}$ grain.
Veratrina	0.002 Gm. = 2 milligrammes.	$\frac{1}{30}$ grain.
Veratrum	0.125 Gm. = 125 milligrammes.	2 grains.
Viburnum Opulus	2 Gm.	30 grains.
Viburnum Prunifolium	2 Gm.	30 grains.
Vinum Antimonii	1 Cc.	15 minims.
Vinum Cocæ	16 Cc.	4 fluidrachms.
Vinum Colechici Seminis	2 Cc.	30 minims.
Vinum Ergotæ	8 Cc.	2 fluidrachms.
Vinum Ferri	8 Cc.	2 fluidrachms.
Vinum Ferri Amarum	8 Cc.	2 fluidrachms.
Vinum Ipecacuanbæ	1 Cc.	15 minims.
Vinum Opii	0.5 Cc.	8 minims.
Xanthoxylum	2 Gm.	30 grains.

Table of average doses, as given by the U. S. Pharmacopœia, eighth decennial revision—Continued.

PREPARATION.	AVERAGE DOSE.	
	Metric System.	Approximate Equivalent Ordinary System.
Zinci Acetas	0. 125 Gm. = 125 milligrammes.	2 grains.
Zinci Bromidum	0. 125 Gm. = 125 milligrammes.	2 grains.
Zinci Iodidum	0. 065 Gm. = 65 milligrammes.	1 grain.
Zinci Oxidum	0. 250 Gm. = 250 milligrammes.	4 grains.
Zinci Phenolsulphonas	0. 125 Gm. = 125 milligrammes.	2 grains.
Zinci Sulphas	1 Gm.	15 grains.
Zinci Valeras	0. 125 Gm. = 125 milligrammes.	2 grains.
Zingiber	1 Gm.	15 grains.

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TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

HYGIENIC LABORATORY.—BULLETIN No. 24.

M. J. ROSENAU, Director.

SEPTEMBER, 1905.

THE INTERNATIONAL CODE
OF
ZOOLOGICAL NOMENCLATURE
AS APPLIED TO
MEDICINE.

BY
CH. WARDELL STILES.



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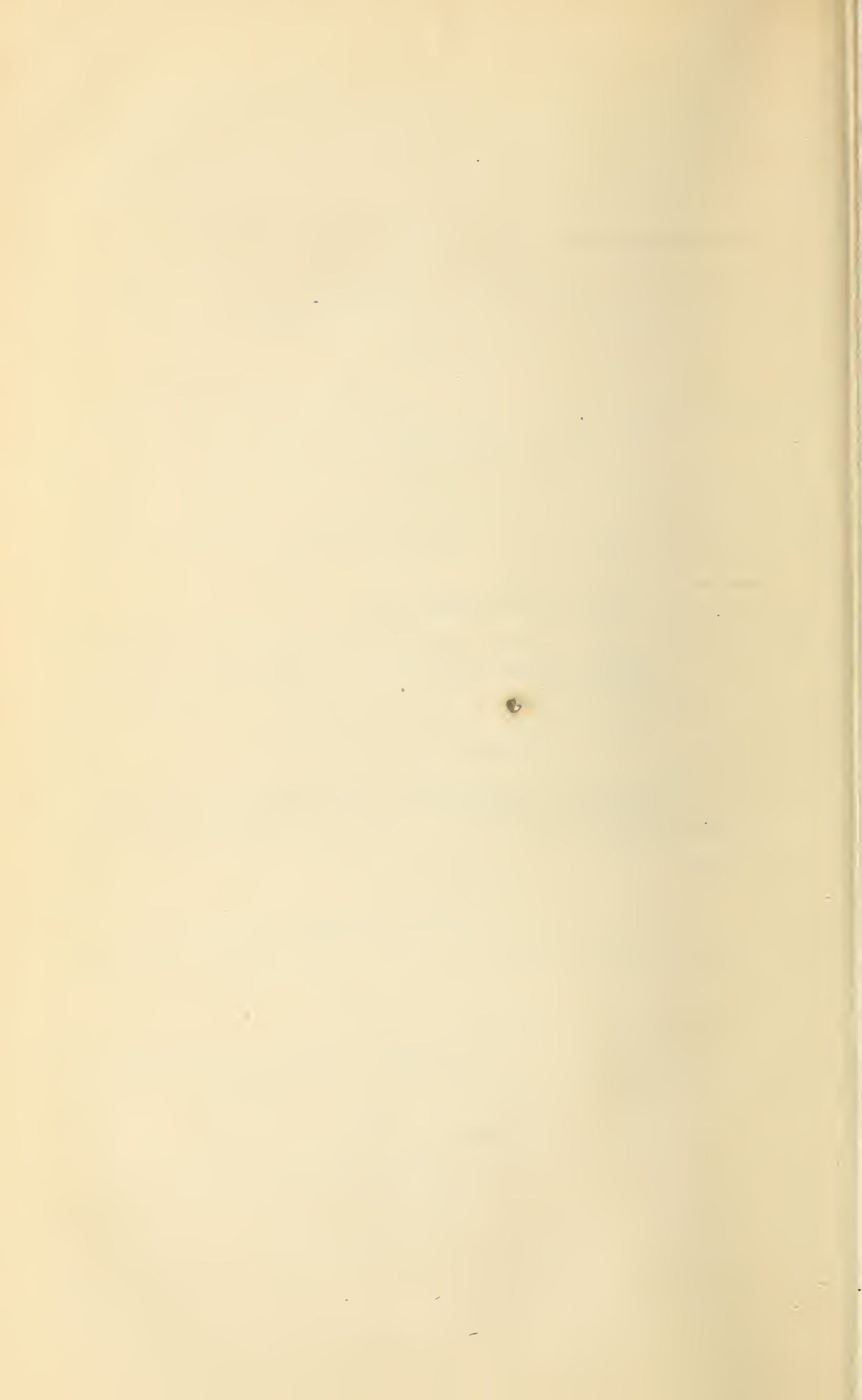
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THE INTERNATIONAL CODE OF ZOOLOGICAL NOMENCLATURE AS APPLIED TO MEDICINE.

By CH. WARDELL STILES, PH. D.,

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INTRODUCTION.

Repeated requests have been made by pathologists, bacteriologists, and zoologists of this country that a bulletin be issued giving the present International Rules of Zoological Nomenclature, explaining their use and practical application, and showing their influence upon the nomenclature used in medicine. In response to these requests the present paper has been prepared.

In treating the subject, the code is given seriatim, as at present in force; under each rule or recommendation explanations and examples are given when necessary. In these explanations, however, I do not discuss the subject in my capacity as secretary of the International Commission, but rather in my professional capacity as a zoologist.

PURPOSE OF THE CODE.—Zoologists are obliged to deal with hundreds of thousands of technical names. In a summary of the animal kingdom Ludwig (1886) estimated that there were then 312,015 known species of animals, divided as follows: Vertebrates, 27,100; tunicates, 300; mollusks, 42,215; molluscoidea, 5,160; arthropods, 212,975; worms, 5,700; echinoderms, 6,210; coelenterates, 6,225; protozoa, 6,130. This estimate must be considered as conservative even for the year 1886.

Ashmead (1895) estimated the number of known species of insects at 284,000, a total which exceeds the estimate made by Ludwig (1886) for all the arthropods (insects, mites, crustaceans, etc.). Howard (1905) has been kind enough to estimate for me the total number of known and unknown species of insects for the world, which he thinks is between 3,500,000 and 4,000,000.

Scudder (1882) collated about 79,000 generic and supergeneric zoological names, and Waterhouse (1902) collected 29,683 additional names. Waterhouse estimates that from 1880 to 1900 about 1,150 new generic and supergeneric zoological names were proposed annually.

It is safe to say that the known genera and species of animals represent but a fraction (not over 10 to 20 per cent) of the zoological names which will come into use during the next two or three centuries, for there are extensive areas of the world which are not yet explored zoologically; and when we consider that even in Europe, where work on systematic zoology has been in progress for a century and a half, hundreds of new genera and species are still becoming known, and when we consider further that we are only beginning to know the parasitic protozoa, it is clear that our nomenclatural tasks are easy, compared with the tremendous number of technical names that future generations will fall heir to.

Under these circumstances it is seen that in order to prevent our science from becoming "a mere chaos of words," every zoological author owes a serious nomenclatural duty not only to himself and his colleagues of to-day, but also to future generations of zoologists.

Linnæus (1751) seems to have appreciated the necessities of his own time, and to no little extent the possibilities of the future, for he proposed a set of rules in accordance with which botanical and zoological names should be used.

If it were left to each author to accept or reject names according to his own personal wishes in the matter, the science of zoology would soon reach a stage in which it would be difficult for one author to understand the writings of another, hence, in order to prevent such a chaotic state, systematists have felt themselves forced to adopt certain rigid rules in accordance with which any given animal shall have only one valid name, and that name shall be valid not only in the country in which it is proposed but in all other lands as well.

The purpose of the International Code of Nomenclature is, therefore, to remove zoological nomenclature from subjective influences and by placing it on an objective basis to make it international; by this plan, a zoologist in South Africa chooses his technical names in accordance with the same rules as does the zoologist in Europe, Asia, Australia, or America.

The code in question deals with nomenclature (namely, with the names of systematic units, such as genera and species), but not with terminology (namely, the names of organs, functions, conditions, etc.).

ORIGIN OF THE INTERNATIONAL CODE.—Reference has already been made to the important fact that Linnæus (1751), the father of modern biological nomenclature, proposed a system of rules of nomenclature. Since it is difficult for one generation to legislate for succeeding generations, it is not strange that later authors discovered that the Linnæan rules, fundamentally good though they were, were not sufficient to meet all the requirements of the advances in the biological sciences, and since the publication (1751) of the Linnæan code various efforts have been made to improve upon the rules he laid down.

Among the most important efforts in this line, mention may be made of the following:

Rudolphi (1801) proposed a set of rules to govern the names of parasites, but he failed to carry out consistently at least one of his most important paragraphs, and much as we owe to Rudolphi for his work in helminthology, work which we all freely admit to be brilliant when judged from the standards of his time, it must be admitted that he has made the nomenclature of parasites rather more involved than would be the case had he been consistent.

One of the most important nomenclatural movements which has ever taken place, and one to which science owes much, was the preparation of the so-called "Stricklandian Code," also known as the "British Association Code" or the "B. A. Code," prepared in 1842-43 by a committee of the British Association for the Advancement of Science. Strange to relate, the American Society of Geologists and Naturalists adopted (1845) this code before it was adopted (1846) by the British Association. For some years American and English zoologists followed this excellent code, which, together with the Linnaean Code (1751) forms the basis of all subsequent study of the subject.

It will be noticed that the Linnaean and Rudolphi codes were proposed by individuals, the former applying to both botany and zoology, the latter only to a restricted group in zoology, while the B. A. Code emanated from a national society of English-speaking scientists. The first movement of an international nature seems to be due to the International Congress of Geology, which in 1881 adopted a code prepared by Douvillé to govern the names of the fossils.

Prior to the Douvillé (1881) code, Dall (1877) prepared a very excellent code at the instance of the American Association for the Advancement of Science, and this set of rules, although never formally adopted by the association, is one of the best essays on the subject that has ever been issued.

The American Ornithologists' Union in 1885 adopted an excellent set of rules, which, known as the "A. O. U. Code," has been followed by many American and foreign zoologists. Excellent as this set of rules is, it rests upon a fundamental theoretical error, so far as general zoological legislation is concerned, namely: This society is a limited society, confined to specialists in a single group, hence zoologists at large had no opportunity to bring forward the difficulties and problems of other groups, and they had no determining vote on the rules in question; under such circumstances, it could hardly be expected that the "A. O. U. Code" should be more than the union claimed for it, namely, a code to govern the scientific names of American birds.

The influence of this code in this country, even in groups other than birds, has been very extensive and very excellent.

To the farseeing judgment of Raphael Blanchard is due the concep-

tion of the International Code. Influenced by the view that it was time to adopt a common code for all groups and for all countries, Blanchard proposed a code which was adopted by the first (1889, Paris) and second (1892, Moscow) International Zoological Congresses. His discussion of the principles involved is classical and his essays will remain standard works of reference. Still, the point has been raised that the work involved was too extensive to be properly considered in all detail in a large audience without previous careful study by a representative committee, and while many authors accepted the rules adopted by the two congresses of 1889 and 1892, other authors failed to follow them.

The German Zoological Society (1894) adopted a code of its own, prepared by a special committee, consisting of Carus, Döderlein, and Möbius, and the German members of that society have followed these rules more or less in detail.

When the Third International Zoological Congress met (1895, Leyden) the situation was practically as follows:

English systematists were following the Stricklandian Code; French systematists were following the International Code; German systematists were following the German Code; American systematists were divided between the Stricklandian, the "A. O. U.," the Dall, and the International codes; systematists in special groups were in some cases following special or even personal codes; and systematists of Italy, Russia, and some other countries were following either the International or some other code.

F. E. Schulze proposed to the Third International Congress (1895, Leyden) that an international commission of five members should be appointed to study all of these codes and to consider their similarities and differences. This proposition was supported by Blanchard, and the following commission was appointed: Prof. R. Blanchard (Paris), Prof. J. V. Carus (Leipzig), Dr. F. A. Jentink (Leyden), Dr. P. L. Sclater (London), and Dr. Ch. Wardell Stiles (Washington).

The commission reported progress at the Fourth International Congress (1898, Cambridge) and was increased to fifteen members. This larger commission reported to the Fifth International Congress (1901, Berlin), and the code proposed was adopted. A subcommittee consisting of Blanchard, von Maehrenthal, and Stiles was then instructed to edit the code in English, French, and German, and this duty was completed at the Sixth Congress (Berne, 1904).

The Berne Congress reorganized the permanent commission so that five of its members retire every three years; as at present constituted it is as follows:

To retire in 1907: Dr. R. Horst (Leyden), Dr. F. A. Jentink (Leyden), President David Starr Jordan (Palo Alto, Cal.), Prof. F. E. Schulze (Berlin), Dr. L. Stejneger (Washington).

To retire in 1910: Prof. R. Blanchard (Paris), Prof. L. Joubin (Paris), Dr. Ch. Wardell Stiles (Washington), Prof. Th. Studer (Berne), Prof. R. R. Wright (Toronto).

To retire in 1913: Mr. Ph. Dautzenberg (Paris), Dr. W. E. Hoyle (Manchester), Prof. L. von Graff (Graz), Prof. F. C. von Maehrenthal (Berlin), Prof. H. O. Osborn (New York).

Executive committee: Professor Blanchard (president), Professor von Maehrenthal (secretary), Doctor Stiles (secretary).

POWERS OF THE INTERNATIONAL COMMISSION.—Under the ruling of the International Congress, no proposition for change in the code is permitted to come before the congress, unless it is presented to the Permanent Commission at least one year before the meeting of the congress. Any person in the world has the right to make any nomenclatural proposition, and this is first considered by the executive committee; this committee studies the proposition and then submits it to the commission; the commission considers it and makes recommendation to the congress, which has the final decision in the matter. By this method of procedure it is intended to provide for any additions to the code which may become necessary, but to protect the code from the introduction of any revolutionary and ill-advised changes.

Thus the commission is a deliberative and advisory body, but has no legislative powers; legislation rests with the congress, and membership in this is open to all persons interested in zoology, regardless of country or special field of work.

It would, accordingly, seem that the general scheme of legislative action is well arranged and that provision is made both to insure conservatism and to provide for progress.

Neither the commission nor the congress has any power to force zoologists and others to adopt the International Rules. Every person is still in a position to follow any code he desires or to prepare one of his own, but, considering the responsibilities involved, there is undoubtedly a growing tendency to adopt the International Code. Further, it is considered ethical to ignore names used contrary to this and to other standard codes.

While not attempting to dictate to men of science what they shall or shall not do, the commission submits the rules to the serious consideration of all workers in the spirit advanced by Strickland (1842), namely, "we offer them to the candid consideration of zoologists in the hope that they may lead to sufficient uniformity of method in future to rescue science from becoming a mere chaos of words."

THE INTERNATIONAL CODE.

GENERAL CONSIDERATIONS.

Article 1. Zoological nomenclature is independent of botanical nomenclature in the sense that the name of an animal is not to be rejected simply because it is identical with the name of a plant. If, however, an organism is transferred from the vegetable to the animal kingdom its botanical names are to be accepted in zoological nomenclature with their original botanical status; and if an organism is transferred from the animal to the vegetable kingdom its names retain their zoological status.

RECOMMENDATION.—It is well to avoid introducing into zoology as generic names such names as are in use in botany.

DISCUSSION.—Some of the earlier codes attempted to cover both botany and zoology, but the present International Code deals only with zoology (hence not with bacteriology). The same general principles apply to both fields, and on account of the lack of a definite line of demarcation between the animals and plants the zoologist is obliged to consider certain relations of botanical to zoological nomenclature.

In not a few cases the same generic name is used without confusion in both botany and zoology. Botanists do not reject a generic name simply because it is used in zoology, nor do zoologists reject a name simply because it is used in botany. Thus, *Balanus*, *Calamus*, *Lunaria*, and a number of other names are used in both zoology and botany. It is, however, wise to avoid the introduction of a new generic name in one kingdom when it is known to have been used in the other.

In some cases an organism has been described as a plant and later investigations have resulted in transferring it to the animals. In these cases zoologists accept the botanical names. Thus, *Plasmodium malarix* was originally (1881) classified in a plant genus as *Oscillaria malarix*. Now that this organism is classified as an animal the original specific name *malarix* (1881) is accepted in zoology with its original botanical date. The generic name *Oscillaria* is not taken over with the specific name because it was not proposed for this organism. *Oscillaria* remains, as it was prior to 1881, a plant genus.

In still other cases organisms have been described as animals and afterwards classified as plants. Thus, *Coccidioides immitis* was provisionally classified with reserve as a sporozoon, but was later placed

among the plants. The generic name, however, having once been used in the animal kingdom for one organism, can not be used for any other organism classified as an animal, despite the fact that the original *Coccidioides* is no longer viewed as an animal. The names *Bacillus*, *Bacterium*, *Spirillum*, *Spirochæta*, and *Vibrio* are of interest in this general connection, since the bacteria were first classified as animals, later as plants, while *Spirochæta* has now been transferred again to zoology.

Spirochæta Ehrenberg, 1834a, 169, was proposed as a genus of protozoa; it was then classified among the plants; more recently it has been returned to the animal kingdom. Although for years this genus was classified among the plants, it still retained its zoological status. This case will illustrate the necessity for the rule given above. Had zoologists admitted *Spirochæta* as valid for some new genus (cf. *Spirochæta* Sars., 1856, a worm) on the ground that the original *Spirochæta* had been eliminated from the animal kingdom, it would now be necessary to change the name of the later *Spirochæta* genus upon the return of *Spirochæta*, 1834, to the animal kingdom.

Art. 2. The scientific designation of animals is uninominal for subgenera and all higher groups, binominal for species, and trinominal for subspecies.

DISCUSSION.—Prior to the introduction of the Linnæan system of nomenclature, organisms were generally given a polynominal name, which in many cases was identical with the description. The Linnæan system introduced into zoology and botany the custom of using two names, hence it is frequently called the “binomial” system. These names referred to two things, or two systematic units (namely, the genus and the species), hence the Linnæan method is frequently known as the “binary” system. One of these names is the *generic* name (corresponding to the family name or surname of persons), the other is the *specific* name (corresponding to the Christian name of persons). Thus, man as a systematic unit is known as *Homo sapiens*; the tiger is *Felis tigris*, the lion *Felis leo*. In the case of the feline animals, *Felis* is the generic name (corresponding to the family name *Smith*), while *tigris* and *leo* are specific names (corresponding to *John*, *Frank*, *Mary*, etc.). When the generic name is combined with a specific name, as *Felis tigris*, the combination is known as the “binomial.”

In some instances it is convenient to recognize a systematic unit of lower value than the species; such units are known as *subspecies*. Thus, the wild boar is known as *Sus scrofa*; but the domesticated hog is recognized as more or less distinct from the boar, yet not sufficiently distinct to be given full specific rank. It is classified as a subspecies, *Sus scrofa domestica*, the combination of the generic, the specific, and the subspecific names representing the “trinomial.”

The use of a trinomial, such as *Sus scrofa domestica* or *Fratercula artica glacialis*, in a subspecific sense should not be confused with expressions like *Bacillus coli communis*. This latter expression can claim no standing in nomenclature, for *communis* was not proposed as a subspecies of any species known as *Bacillus coli*.

Turning now to zoological names used by physicians, it should be noticed that *Tænia*, *Plasmodium*, *Amæba*, *Culex*, *Stegomyia*, *Bacillus*, *Bacterium*, etc., are generic names, while *Tænia saginata*, *Plasmodium malarix*, *Amæba coli*, *Culex pipiens*, *Stegomyia fasciata*, *Bacillus icteroides*, *Bacterium anthracis*, etc., are binomials applied to species, and *Tænia solium abietina* was used as a trinomial for a supposed variety of *Tænia solium*.

In order that names may claim recognition, they must always be proposed in the sense given above, and unless they are proposed in the manner indicated they are not considered in establishing the correct name for any systematic unit. Thus *Filaria sanguinis hominis nocturna* is a polynomial applied to a species, hence it has no status in nomenclature; we may of course quote it as a matter of historic interest or in a bibliographic citation, but in determining the correct name of the animal to which it was applied the name is to be completely ignored.

Art. 3. The scientific names of animals must be words which are either Latin or Latinized, or considered and treated as such in case they are not of classic origin.

DISCUSSION.—The adoption of Latin names rests both upon the historical development of nomenclature and upon practical considerations. Earlier scientific authors wrote in Latin, hence they naturally used Latin names, and these have been preserved by more recent authors.

The chief object of the use of Latin names is based upon practical considerations. Assuming that there are 10,000,000 species of animals in the world (assuredly an ultraconservative estimate), it would be a practical impossibility to keep record of them unless international names were used. If we had to record for each of these 10,000,000 species an English, French, German, Italian, Russian, and perhaps a Japanese and a Chinese name, zoology would consist chiefly of a study of languages. It is not considered a practical proposition to attempt to adopt any modern language as basis for the names, as questions of national pride would arise which would doubtless exclude any agreement. But every nation which studies zoology also studies Latin to a greater or less extent, and by adopting Latin no one nationality is called upon to make any greater concessions than is any other.

Nothing is stated in the rule as to what particular Latin should be used, but latitude is granted to use Latin or Latinized names, or to use names as if they were Latin. This latitude has its practical basis.

The Latin poets and authors did not foresee the practical scientific use to which their language would be applied, and they failed to leave enough Latin words as names for the millions of animals and plants which come into consideration. Hence, as a carpenter, a sailor, or a manufacturer coins words which are accepted in English as English words of good standing, when applied to carpentry, nautical affairs, and trade, the zoologists and botanists coin words upon Latin precedents, which we adopt as botanical and zoological Latin. In not all cases do our efforts attain the highest standards of classical Latin (*Tænia solium*, and *Gadus tomcod*, for instance), but because of practical considerations such names are retained, although not recommended as examples to be followed in coining new words.

As an instance in which zoologists take considerable liberty with Latin special mention may be made of the family and subfamily names, the rule for their formation being based upon practical considerations rather than upon classical precedent.

Many authors have used vernacular names in a vernacular sense without giving a Latin equivalent. This is particularly the case with certain earlier French authors. Later authors have not infrequently Latinized these vernacular names and the Latinized form has been adopted. In all these cases the vernacular names have no status whatever in nomenclature, and the author who later Latinized the name or used it as a Latin name is the person who is considered its author. Thus Redon, 1883, described for man a "*Tænia algérien*," which Pepper (1894) has quoted as *Tænia algeriana* and Braun (1894) as *Tænia algeriensis*. In this case *Tænia algérien* is a vernacular name, and its author (Redon) is in no wise connected with the names *Tænia algeriana* and *T. algeriensis*, which should be attributed to Pepper and Braun, respectively, despite the fact that it was Redon who described the parasite. In following this plan we are not attempting to rob Redon of any supposed credit which belongs to him, but we do not hold him responsible for names introduced by later authors.

FAMILY AND SUBFAMILY NAMES.

Art. 4. The name of a family is formed by adding the ending *idæ*, the name of a subfamily by adding *inæ*, to the root of the name of its type genus.

DISCUSSION.—Closely related genera are collected into families, and when desirable an intermediate systematic unit (the subfamily) is recognized between the genus and the family; in other words, closely related genera are collected into subfamilies and closely related subfamilies are collected into families.

One genus in each subfamily represents the type of the subfamily, namely, its standard of reference; and one genus in the family represents the standard of reference of the family. In forming the family

and subfamily names the name of the type genus is taken as basis, and the endings *idæ* and *inæ* are added to the root of the generic name in question. Thus the tapeworms in man are classified as follows:

Family *Tæniidæ*, based upon *Tænia* as its type genus.

Subfamily *Tæniinæ*, based upon *Tænia* as its type genus.

Genera *Tænia* and *Echinococcus*.

Subfamily *Dipylidiinæ*, based upon *Dipylidium* as its type genus.

Genera *Dipylidium* and *Hymenolepis*.

Subfamily *Davaineinæ*, based upon *Davainea* as its type genus.

Family *Dibothriocephalidæ*, based upon *Dibothriocephalus* as its type genus.

Subfamily *Dibothriocephalinæ*, based upon *Dibothriocephalus* as its type genus.

Genera *Dibothriocephalus*, *Diplogonoporus*, and *Sparganum*.

A moment's consideration will show that this method of forming family and subfamily names is based upon practical considerations; by having a uniform set of endings we know that any name ending in *idæ* is of family rank, while one ending in *inæ* is of subfamily rank. Further, by using a prominent generic name as basis for the family and subfamily names we aid the memory in locating the systematic position of the groups.

Art. 5. The name of a family or subfamily is to be changed when the name of its type genus is changed.

DISCUSSION.—While one of the fundamental purposes of the code is to prevent an *unnecessary* change of names, it is considered that under certain circumstances changes must be made for the general good. As illustrating such an event, and as explaining article 5, the following example may be taken:

“*Distoma hepaticum*” is a parasite mentioned in most works on practice of medicine; it is frequently classified in the family “*Distomidæ*,” of which it forms the “type.” The correct name of this parasite is *Fasciola hepatica*, and upon suppressing the generic name *Distoma*, in favor of *Fasciola*, the family name *Distomidæ* is changed to *Fasciolidæ*. Were this change not made, we should be obliged to carry in our minds a family name (*Distomidæ*) and a subfamily name (*Distominæ*) without any direct clue as to their systematic position; further, in this and in many other instances confusion would arise between the family name of this group of parasitic worms, and a family name used for an entirely different set of animals.

GENERIC AND SUBGENERIC NAMES.

Art. 6. Generic and subgeneric names are subject to the same rules and recommendations, and from a nomenclatural standpoint they are coordinate, that is, they are of the same value.

DISCUSSION.—The question as to whether a given systematic unit should be given generic or subgeneric rank, is to no little extent sub-

jective, and our ideas change in regard to a given case as our knowledge of the group increases. Hence, we treat generic and subgeneric names *nomenclaturally* as of the same rank and as interchangeable.

Thus, most authors recognize that *Tænia* is to be divided into the subgenera *Tænia*, *Multiceps* (i. e., *Cœnurus*), and *Echinococcus*. Some authors, however, incline to recognize these subgenera as of full generic rank. By subjecting both generic and subgeneric names to the same rules, and granting them equal rank from a *nomenclatural* point of view, regardless of the recognized systematic point of view, confusion is lessened, and we gradually become accustomed to associating certain species together in groups, to which generic rank may later be given.

Art. 7. A generic name becomes a subgeneric name, when the genus so named becomes a subgenus, and vice versa.

DISCUSSION.—If an author, in revising the genus *Tænia*, concludes that the subgenera *Multiceps* and *Echinococcus* should be given generic rank, he is called upon to use these subgeneric names as names of the genera he recognizes; if a later author differs in opinion and reduces these genera to subgenera, he still retains the same names as names of his subgenera.

This rule is based upon a fundamental principle of nomenclature too frequently overlooked, namely, *in naming a systematic unit we name the object, not our concept of the object*. If we name a given genus, we do not confine the name to the animals which come within *our* description of the genus, but we propose a generic name to be used for all animals which agree generically with our type species, be they known to us or not; some later author may have a different concept of the extent of the genus, but as long as he classifies species generically with the species which we have designated as the generic type, our generic name—even if used originally in a more restricted or a less restricted sense—is valid, provided it fulfills all the conditions demanded of it by the code.

Art. 8. A generic name must consist of a single word, simple or compound, written with a capital initial letter, and employed as a substantive in the nominative singular. Examples: *Canis*, *Perca*, *Ceratodus*, *Hymenolepis*.

DISCUSSION.—It is quite a common occurrence to find in medical writings “*bacillus tuberculosis*,” “*plasmodium malarix*,” “*amæba coli*,” “*tænia solium*,” etc., the generic names being written with small initial letter. Zoologists and botanists adopt a capital initial letter for the generic name, because of the aid this gives them in quickly recognizing the rank of the name; thus, if we find “*Heterophyes*,” we know that reference is made to a certain genus of flukes, one species of which occurs in man; if we find *heterophyes* used in a paragraph in which *Heterophyes* is discussed, we know that *heterophyes*

refers, not to the genus as a whole, but to the particular species that occurs in man. This custom of capitalizing the generic name has come down to us from former centuries, and while it now has its practical basis, its historic basis is probably due to the custom earlier authors had of capitalizing all Latin substantives when used in nomenclature. At present the custom is so thoroughly established that botanists and zoologists experience much the same sensation in seeing "*bacillus tuberculosis*" or "*plasmodium malariae*," instead of *Bacillus tuberculosis* and *Plasmodium malariae*, that they would if they found a reference to "american" authors or to "doctor s. weir mitchell."

RECOMMENDATIONS.—The following words may be taken as generic names:

a. Greek substantives, for which the rules of Latin transcription (see Appendix F) should be followed. Examples: *Ancylus*, *Amphibola*, *Aplysia*, *Pompholyx*, *Physa*, *Cylichna*.

b. Compound Greek words, in which the attributive should precede the principal word. Examples: *Stenogyra*, *Pleurobranchus*, *Tylodina*, *Cyclostomum*, *Sarcocystis*, *Pelodytes*, *Hydrophilus*, *Rhizobius*.

This does not, however, exclude words formed on the model of *Hippopotamus*, namely, words in which the attributive follows the principal word. Examples: *Philydrus*, *Biorhiza*.

c. Latin substantives. Examples: *Ancilla*, *Auricula*, *Dolium*, *Harpa*, *Oliva*. Adjectives (*Prasina*) and passed participles (*Productus*) are not recommended.

d. Compound Latin words. Examples: *Stiliger*, *Dolabrifer*, *Semifusus*.

e. Greek or Latin derivatives expressing diminution, comparison, resemblance, or possession. Examples: *Dolium*, *Doliolum*; *Strongylus*, *Eustrongylus*; *Limax*, *Limacella*, *Limacia*, *Limacina*, *Limacites*, *Limacula*; *Lingula*, *Lingulella*, *Lingulepis*, *Lingulina*, *Lingulops*, *Lingulopsis*; *Neomenia*, *Proneomenia*; *Buteo*, *Archibuteo*; *Gordius*, *Paragordius*, *Polygordius*.

f. Mythological or heroic names. Examples: *Osiris*, *Venus*, *Brisinga*, *Velleda*, *Crimora*. If not Latin, these should be given a Latin termination (*Aegirus*, *Göndolia*).

g. Proper names used by the ancients. Examples: *Cleopatra*, *Belisarius*, *Melania*.

h. Modern patronymics, to which is added an ending to denote dedication:

α. Names terminating with a consonant take the ending *ius*, *ia*, or *ium*. Examples: *Selysius*, *Lamarckia*, *Köllikeria*, *Mülleria*, *Stålia*, *Krøyeria*, *Ibañezia*.

β. Names terminating with the vowels *e*, *i*, *o*, *u*, or *y* take the ending *us*, *a*, or *um*. Examples: *Blainvillea*, *Wyrillea*, *Cavolinia*, *Fatioa*, *Bernaya*, *Quoya*, *Schulzea*.

γ. Names terminating with *a* take the ending *ia*. Example: *Danaia*.

δ. In generic names formed from patronymics, the particles are omitted if not coalesced with the name, but the articles are retained. Examples: *Blainvillea*, *Benedenia*, *Chiajea*, *Lacepedea*, *Dumerilia*.

ε. With patronymics consisting of two words, only one of these is used in the formation of a generic name. Examples: *Selysius*, *Turgionia*, *Edwardsia*, *Duthiersia*.

ζ. The use of proper names in the formation of compound generic names is objectionable. Examples: *Eugrimmia*, *Buchiceras*, *Heromorpha*, *Möbiusispongia*.

i. Names of ships which should be treated the same as mythological names (*Vega*) or as modern patronymics. Examples: *Blakea*, *Hirondellea*, *Challengeria*.

j. Barbarous names, that is, words of nonclassic origin. Examples: *Vanikoro*, *Chilosa*. Such words may receive a Latin termination. Examples: *Yetus*, *Fossarus*.

k. Words formed by an arbitrary combination of letters. Examples: *Neda*, *Clanculus*, *Salifa*, *Torix*.

l. Names formed by anagram. Examples: *Dacelo*, *Verlusia*, *Linospa*.

DISCUSSION.—A person who is not accustomed to dealing with a large number of generic names, and even authors who are well trained in the subject, frequently find it difficult to coin or to select names for new genera. To aid them in their labors, the foregoing recommendations, based upon an analysis of thousands of names already in use, have been inserted into the code.

Art. 9. If a genus is divided into subgenera, the name of the typical subgenus must be the same as the name of the genus (see Art. 25).

DISCUSSION.—Subgenera are used in zoology by a number of authors, but other authors avoid them. Not infrequently it will be noticed that the species of a given genus may be classified into several natural groups, to which an author does not feel justified at the moment in giving full generic rank; to express the systematic relations of these species and groups an author may recognize subgenera. One of these subgenera naturally contains the type species of the genus, and this is known as the typical subgenus. Unfortunately, some authors have proposed new names for the typical subgenera, but the law of priority (Art. 25) demands that the typical subgenus must have the same name as the genus itself.

Thus *Tænia* has been divided into the following subgenera: *Tænia*, type *solium*; *Multiceps* (or *Cænurus*), type *cerebralis*; *Echinococcus*, type *echinococcus*=*granulosus*. Some authors have recognized *Cystotænia* as the name of the typical subgenus, but this is inadmissible under the code. By using *Tænia* instead of *Cystotænia* the nomenclature remains the same in the writings of those authors who recognize subgenera and those who raise subgenera to generic rank.

Art. 10. When it is desired to cite the name of a subgenus, this name is to be placed in parentheses between the generic and the specific names. Example: *Vanessa* (*Pyrameis*) *cardui*.

DISCUSSION.—Even when subgenera are recognized it is not necessary to quote the subgeneric name every time the species are cited, but if the subgeneric name is quoted it should be placed in parentheses. Some authors have used the parenthesis in a different and somewhat confusing manner; not infrequently a well-known genus is split up into distinct genera and an author occasionally cites the old generic name to show the former position of the species. Thus we find references like *Hymenolepis* (*Tænia*) *nana*, the author meaning that he classifies *Tænia nana* as *Hymenolepis nana*. It is much better in these cases to write [*Tænia*] *Hymenolepis nana*, thus avoiding the appearance of making *Tænia* a subgenus of *Hymenolepis*.

SPECIFIC AND SUBSPECIFIC NAMES.

Art. 11. Specific and subspecific names are subject to the same rules and recommendations, and from a nomenclatural standpoint they are coordinate—that is, they are of the same value.

DISCUSSION.—See under article 6.

Art. 12. A specific name becomes a subspecific name when the species so named becomes a subspecies, and vice versa.

DISCUSSION.—See under article 7.

Art. 13. While specific substantive names derived from names of persons may be written with a capital initial letter, all other specific names are to be written with a small initial letter. Examples: *Rhizostoma Cuvieri* or *Rh. cuvieri*, *Francolinus Lucani* or *F. lucani*, *Hypoderma Diana* or *H. diana*, *Laophonte Mohammed* or *L. mohammed*, *Æstrus ovis*, *Corvus corax*.

DISCUSSION.—Formerly all substantive specific names were capitalized, while most adjectival specific names were written with a small initial letter. Then the custom relative to specific names changed to confining the capital to names derived from proper names. Later the capitals were restricted to names derived from names of persons, and finally the use of capitals in specific names was entirely rejected, except that names derived from names of persons *may* be written with a capital. The use of the capital is a convenience in distinguishing between a specific name like *Gobii*, based upon the surname *Gobi*, and a specific name *gobii* based upon the generic name *Gobius*. There is now a decided tendency to reject the use of capitals in specific names.

Art. 14. Specific names are:

a. Adjectives, which must agree grammatically with the generic name. Example: *Felis marmorata*.

b. Substantives in the nominative in apposition with the generic name. Example: *Felis leo*.

c. Substantives in the genitive. Examples: *rosæ*, *sturionis*, *antillarum*, *galliæ*, *sancti-pauli*, *sanctæ-helenæ*.

If the name is given as a dedication to one or several persons, the genitive is formed in accordance with the rules of Latin declination in case the name was employed and declined in Latin. Examples: *Plinii*, *Aristotelis*, *Victoris*, *Antonii*, *Elisabethæ*, *Petri* (given name).

If the name is a modern patronymic, the genitive is always formed by adding, to the exact and complete name, an *i* if the person is a man, or an *æ* if the person is a woman, even if the name has a Latin form; it is placed in the plural if the dedication involves several persons of the same name. Examples: *Cuvieri*, *Möbiusi*, *Nuñezi*, *Merianæ*, *Sarasinorum*, *Bosi* (not *Bovis*), *Salmoni* (not *Salmonis*).

RECOMMENDATION.—The best specific name is a Latin adjective, short, euphonic, and of easy pronunciation. Latinized Greek words or barbarous words may, however, be used. Examples: *gymnocephalus*, *echinococcus*, *ziczac*, *aguti*, *hoactli*, *urubitinga*.

Art. 15. The use of compound proper names indicating dedication, or of compound words indicating a comparison with a simple object, does not form an exception to Art. 2. In these cases the two words composing the specific name are written as one word with or without the hyphen. Examples: *sanctæ-catharinæ*, or *sanctæcatharinæ*, *jan-mayeni* or *janmayeni*, *cornu-pastoris* or *cornupastoris*, *cor-anguinum* or *coranguinum*, *cedo-nulli* or *cedonulli*.

Expressions like *rudis planusque* are not admissible as specific names.

Art. 16. Geographic names are to be given as substantives in the genitive, or are to be placed in an adjectival form. Examples: *sancti-pauli*, *sanctæ-helenæ*, *edwardiensis*, *diemenensis*, *magellanicus*, *burdigalensis*, *vindobonensis*.

RECOMMENDATION.—Geographic names used by the Romans or by Latin writers of the middle ages are to be adopted in preference to more recent forms. Words like *bordeausiacus* and *viennensis* are poor, but are not to be rejected on this account.

Art. 17. If it is desired to cite the subspecific name, such name is written immediately following the specific name, without the interposition of any mark of punctuation. Example: *Rana esculenta marmorata* Hallowell, but not *Rana esculenta (marmorata)* or *Rana marmorata* Hallowell.

Art. 18. The notation of hybrids may be given in several ways; in all cases the name of the male parent precedes that of the female parent, with or without the sexual signs:

a. The names of the two parents are united by the sign of multiplication (\times). Example: *Capra hircus* ♂ \times *Ovis aries* ♀ and *Capra hircus* \times *Ovis aries* are equally good formulæ.

b. Hybrids may also be cited in form of a fraction, the male parent forming the numerator and the female parent the denominator.

Example: $\frac{Capra\ hircus}{Ovis\ aries}$. This second method is in so far preferable that it permits the citation of the person who first published the hybrid form as such. Example: $\frac{Bernicla\ canadensis}{Anser\ cygnoides}$ Rabé.

c. The fractional form is also preferable in case one of the parents is itself a hybrid. Example: $\frac{Tetrao\ tetrix \times Tetrao\ urogallus}{Gallus\ gallus}$. In the latter case, however, parentheses may be used. Example: $(Tetrao\ tetrix \times Tetrao\ urogallus) \times Gallus\ gallus$.

d. When the parents of the hybrid are not known as such [parents], the hybrid takes provisionally a specific name, the same as if it were a true species, namely, as if it were not a hybrid; but the generic name is preceded by the sign of multiplication. Example: $\times Coregonus\ dolosus$ Fatio.

FORMATION, DERIVATION, AND ORTHOGRAPHY OF ZOOLOGICAL NAMES.

Art. 19. The original orthography of a name is to be preserved unless an error of transcription, a *lapsus calami*, or a typographical error is evident.

RECOMMENDATION.—For scientific names it is advisable to use some other type than that used for the text. Example: *Rana esculenta* Linné, 1758, lives in Europe.

DISCUSSION.—The question of emendation of names has been one of the most difficult that has come up for consideration. Some authors, known as “purists,” have insisted upon a classical Latin; others have accepted the original orthography of a name, be it good, bad, or indifferent. Names have been published in a form not altogether in accordance with classical rules, and later authors have emended them; unfortunately, the emending authors have not been in accord in regard to the emendations, and a given name may appear in literature in several “corrected” forms. *Agchylostoma*, for instance, has been “emended” six or eight different times, and it is stated that one name has been “corrected” 23 different times. Unfortunately, also, the emendation of names occasionally leads to the rejection of names which might be retained if emendation were not admitted.

Art. 20. In forming names derived from languages in which the Latin alphabet is used, the exact original spelling, including diacritic marks, is to be retained. Examples: *Selysius*, *Lamarckia*, *Köllikeria*, *Mülleria*, *Stålia*, *Kroyeria*, *Ibañezia*, *Möbinsi*, *Mediçi*, *Čížžeki*, *spitzbergensis*, *islandicus*, *paraguayensis*, *patagonicus*, *barbadensis*, *füröensis*.

RECOMMENDATIONS.—The prefixes *sub* and *pseudo* should be used only with adjectives and substantives, *sub* with Latin words, *pseudo* with Greek words, and they should not be used in combination with proper names. Examples: *subviridis*, *subchelatus*, *Pseudacanthus*, *Pseudophis*, *Pseudomys*. Words like *subwilsoni* and *pseudograteloupana* are not recommended.

The terminations *oides* and *ides* should be used in combination only with Greek or Latin substantives; they should not be used in combination with proper names.

Geographic and patronymic names from countries which have no recognized orthography or which do not use the Latin alphabet should be transcribed into Latin according to the rules adopted by the Geographic Society of Paris (see Appendix G).

AUTHOR'S NAME.

Art. 21. The author of a scientific name is that person who first publishes the name in connection with an indication, a definition, or a description, unless it is clear from the contents of the publication that some other person is responsible for said name and its indication, definition, or description.

DISCUSSION.—At first thought this rule appeals to many persons as unjust. Thus Smith & Kilborne described the parasite of Texas fever

as *Pyrosoma*, 1893; this name, however, had been used by Péron in 1804 for an entirely different group of animals, hence it was not available as name for the Texas fever organism. Wandolleck (1895), on this account, proposed *Apiosoma* to replace *Pyrosoma*, 1893; this name also was preoccupied, in 1885, for a genus of ciliated protozoa: Patton (1895) proposed *Piroplasma* as a substitute for *Pyrosoma*, 1893. The point is advanced by some authors that *Piroplasma* should be attributed to Smith & Kilborne instead of to Patton, as it was Smith & Kilborne, instead of Patton, who described the parasite.

This argument does not appeal to zoologists. Our position is that Smith & Kilborne are responsible for *Pyrosoma*, 1893, but not for *Apiosoma*, 1895, or *Piroplasma*, 1895, and an author should be quoted only for a name for which he is responsible. The act of naming an animal is not identical with the act of describing an animal. We therefore quote Smith & Kilborne for the acts for which they are responsible, but we do not quote them as authority for acts for which they are not responsible. If the policy were adopted that the person who describes an animal should be quoted in connection with all the names that have been applied to it, we would be led to the peculiar position of attributing 110 or more names to Goeze in connection with the parasite of hydatid disease, although most of these names were not published until years after Goeze's death; further, such quotation might entirely misrepresent an author's views. Zoologists are held responsible for the many typographical errors and variations in spelling of technical names, even when—as is very frequently the case—these errors are due entirely to the printer or to an editor who follows some special rules of editing; this responsibility we bear with equanimity, irritating though these errors may be, but to assume responsibility for a dozen or a score of names which we never even thought of is a position which no zoologist cares to defend.

This point of view lays stress upon holding an author responsible for the names he publishes, rather than upon "giving him credit" for these names.

The chief idea we have in citing the author of a name is to aid in tracing it. If now we cited Smith & Kilborne, instead of Wandolleck, as author of *Apiosoma*, or instead of Patton as author of *Piroplasma*, we might lead our colleagues to search long in writings of Smith & Kilborne for a name which they perhaps never used even in correspondence.

Art. 22. If it is desired to cite the author's name, this should follow the scientific name without interposition of any mark of punctuation; if other citations are desirable (date, *sp. n.*, *emend.*, *sensu stricto*, etc.), these follow after the author's name, but are separated from it by a comma or by parentheses. Examples: *Primates* Linné, 1758, or *Primates* Linné (1758).

RECOMMENDATION.—When the name of the author of a scientific name is abbreviated, the writer will do well to conform to the list ^a of abbreviations published by the Zoological Museum of Berlin.

DISCUSSION.—Since authors' names are cited as aids in bibliographic work, it follows that they should not be cited in a manner to render such work more difficult. Thus, if abbreviations are used—their use in connection with authors' names is not to be recommended—an abbreviation should be used which is not ambiguous. “Cob.,” for instance, is unfortunately used for both Cobb and Cobbold.

Art. 23. When a species is transferred to another than the original genus or the specific name is combined with any other generic name than that with which it was originally published, the name of the author of the specific name is retained in the notation but placed in parentheses. Examples: *Tænia lata* Linné, 1758, and *Dibothriocephalus latus* (Linné, 1758); *Fasciola hepatica* Linné, 1758, and *Distoma hepaticum* (Linné, 1758).

If it is desired to cite the author of the new combination, his name follows the parentheses. Example: *Limnatis nilotica* (Savigny, 1820) Moquin-Tandon, 1826.

DISCUSSION.—If a species is transferred from one genus to another, the generic name is of course changed, but the old specific name, if valid, is retained. When *Tænia lata* is transferred to *Dibothriocephalus*, we must of course drop *Tænia* (for this species) in favor of *Dibothriocephalus*, but *lata* becomes *latus*. The case is very much like that of a woman named “Mary Jones,” who by marrying into the Smith family becomes “Mary Smith.”

In all such transfers of species the original author responsible for the specific name is to be cited in parentheses. Thus “*Dibothriocephalus latus* (Linnæus, 1758) Lühe, 1899,” means to the zoologist that Linnæus, in 1758, described a species under the name *latus*, -a, -um, but not as *Dibothriocephalus latus*; further, that Lühe quoted this species as *Dibothriocephalus latus* in 1899.

Art. 24. When a species is divided, the restricted species to which the original specific name of the primitive species is attributed may receive a notation indicating both the name of the original author and the name of the reviser. Example: *Tænia solium* Linné, partim, Goeze.

DISCUSSION.—As different groups of animals become better known, it is common experience to find that what was once considered to represent a single species may in fact contain several distinct species. In separating these various forms, the original name is retained for one of them. Thus *Tænia solium* Linnæus, 1758, contained three species, namely, *T. solium*, *T. saginata*, and *T. hydatigena* (*T. marginata*). *T. solium* of to-day therefore represents only a restricted part of *Tænia solium* as known to Linnæus, 1758.

^a Liste der Autoren zoologischer Art- und Gattungsnamen zusammengestellt von den Zoologen des Museums für Naturkunde in Berlin. Berlin, 2. vermehrte Auflage, 8°, 1896.

THE LAW OF PRIORITY.

Art. 25. The valid name of a genus or species can be only that name under which it was first designated on the condition:

a. That this name was published and accompanied by an indication, or a definition, or a description; and

b. That the author has applied the principles of binary nomenclature.

DISCUSSION.—The law of priority is the keystone of nomenclature. Various attempts have been made to introduce substitutes for it, but none have succeeded.

The point is not infrequently raised that not all zoologists favor this law. To this reply may be made that all persons who have studied the subject carefully see in this law the only hope for an international and stable nomenclature. It is especially the systematists, namely, the men who have to deal with tens of thousands of names, who have insisted upon its adoption; that some physiologists and morphologists (who have to deal with a few score, or a few hundred, at most a few thousand names) should oppose this law is not strange, for their field of study has not been in the line in which the necessity for the law has come home to them. But we do not go to a gynecologist to obtain an opinion on the question whether we should wear glasses nor to an alienist in case we have appendicitis. By following the advice of the ophthalmologist in reference to our eyes, and of the surgeon in reference to appendicitis, we cast no reflections upon the ability of men in other specialties, but we go for advice to men who have had particular experience in the particular line in which we wish the advice. In nomenclatural matters, we naturally turn to the systematists, and they are practically unanimous in favor of the law of priority. In accordance with this law we do not inquire which of the 110 or more names for the echinococcus worm is the most euphonic, the most classical, the most generally used, the easiest to remember, the one of American or of Chinese origin; we simply inquire: Which is the oldest available generic name and the oldest specific name? A combination of these two gives us the correct binomial, regardless of our subjective views on the question. A few practical examples may be of interest in this connection.

Tænia was described in 1758, with four species, as follows:

1. *solium*, which is now divided into
 - (a) *solium*, for which about 90 names have been used;
 - (b) *saginata*, for which about 50 names have been used;
 - (c) *hydatigena*, for which about 40 names have been used.
2. *vulgaris*=same as 3.
3. *lata*, now *Dibothriocephalus lata*, for which about 30 names have been used.
4. *canina*, now *Dipylidium caninum*, for which more than 15 names have been used.

Reduced to the last analysis, the systematists see themselves forced to adopt the oldest available name in any given case, or to leave it to the personal wishes of every author to use any name he prefers. The author who prefers the latter alternative can not, however, consistently criticise an author who "prefers" to use the earliest available name.

Thus, we use *Ascaris*, 1758, in preference to *Fusaria*, 1800; *Tænia saginata*, 1782, in preference to *Tænia mediocanellata*, 1852; *Tænia*, 1758, in preference to *Alyselminthus*, 1800, and *Halysis*, 1803; *Plasmodium malarix*, 1881, in preference to *Plasmodium golgii*, 1902; etc.

APPLICATION OF THE LAW OF PRIORITY.

Art. 26. The tenth edition of Linné's *Systema naturæ*, 1758, is the work which inaugurated the consistent general application of the binary nomenclature in zoology. The date 1758, therefore, is accepted as the starting point of zoological nomenclature and of the law of priority.

DISCUSSION.—The adoption of the tenth edition of the *Systema naturæ* has its practical basis, namely, this was the first work in which the binominal system was consistently applied to all known animals, hence all groups in zoology have the same date (1758) as starting point for their nomenclature. Any earlier names used as generic or specific names in that edition take the date of 1758, while earlier names reintroduced into zoology after January 1, 1758, take priority from such date of reintroduction.

Art. 27. The law of priority obtains and consequently the oldest available name is retained:

- a.* When any part of an animal is named before the animal itself;
- b.* When the larva is named before the adult;
- c.* When the two sexes of an animal have been considered as distinct species or even as belonging to distinct genera;
- d.* When an animal represents a regular succession of dissimilar generations which have been considered as belonging to different species or even to different genera.

DISCUSSION.—Article 27 is of considerable importance in medicine since names of "larval" forms (or alternating generations) as well as names of adults must be considered. Thus, *Echinococcus*, 1801, must take precedence over *Echinococcifer*, 1858, although the former was established upon a "larval" stage, the latter upon a sexually mature stage.

Art. 28. A genus formed by the union of two or more genera or subgenera takes the oldest valid generic or subgeneric name of its components. If the names are of the same date, that selected by the first reviser shall stand.

The same rule obtains when two or more species or subspecies are united to form a single species or subspecies.

RECOMMENDATION.—In absence of any previous revision, the establishment of precedence by the following method is recommended:

(a) A generic name accompanied by specification of a type has precedence over a name without such specification. If all or none of the genera have types specified, that generic name takes precedence the diagnosis of which is most pertinent.

(b) A specific name accompanied by both description and figure stands in preference to one accompanied only by a diagnosis or only by a figure.

(c) Other things being equal, that name is to be preferred which stands first in the publication (page precedence).

DISCUSSION.—The genus *Tænia*, 1758, as at present constituted, is composed of a union of the genera *Tænia*, 1758, *Hydatigena*, 1782, *Megocephalos*, 1782, *Vesicaria*, 1788, *Hydatula*, 1790, *Alyselminthus*, 1800, *Halysis*, 1803, *Physchiosoma*, 1809, *Hydatigera*, 1816, *Trachelocampylus*, 1847, *Arynchotænia*, 1850, *Acanthotrias*, 1858, *Tæniarhynchus*, 1858, *Cystotænia*, 1863, and *Neotenia*, 1886; opinion might differ in regard to which name should be used, but by the law of priority and by article 28 *Tænia* is the correct name for the genus which contains *T. solium*.

The species *Tænia saginata*, 1782, as at present constituted, is composed of several forms which were originally described as distinct.

Hymenolepis, 1858, is composed of a union of *Hymenolepis*, 1858, *Diplacanthus*, 1858, *Lepidotrias*, 1858, and *Drepanidotænia*, 1892.

Art. 29. If a genus is divided into two or more restricted genera, its valid name must be retained for one of the restricted genera.

If a type was originally established for said genus, the generic name is retained for the restricted genus containing said type.

DISCUSSION.—A division of a given genus into more restricted genera is a natural result of our advance in anatomical knowledge. Linnæus in 1758 included in *Tænia* species which are now classified in three more restricted genera. Instead of proposing three new names for these more restricted groups the original name is retained for one of them, namely, for the group which contains the type (*T. solium*). *Fasciola*, 1758, is now divided into a large number of genera, but the fact that *Fasciola* as used to-day is not so broad a genus as when used by Linnæus does not constitute sufficient ground for rejecting this name.

The problem presented is almost the same as that of typhoid fever in 1860, when Zenker recognized that a distinct clinical entity (trichinosis) had been included in typhoid. The newly recognized disease is now called trichinosis, but typhoid is still used for a part of the old composite malady.

If a genus has no type species, and if the genus is divided, it not infrequently occurs that different authors apply the original generic name to different subdivisions of the original genus, and confusion in

the nomenclature results. But if a type is designated, the original generic name always follows the subdivision containing the type, so that uniformity in the generic nomenclature is ensured.

Art. 30. If the original type of a genus was not indicated, the author who first subdivides the genus may apply the name of the original genus to such restricted genus or subgenus as may be judged advisable, and such assignment is not subject to subsequent change.

In no case, however, can the name of the original genus be transferred to a group containing none of the species originally included in the genus; nor can a species be selected as type which was not originally included in the genus or which the author of the generic name doubtfully referred to it.

RECOMMENDATION.—In selecting a type authors should govern themselves by the following:

(a) A genus which contains a species bearing the same name, either as a valid name or as a synonym, takes that species as type.

(b) Select as type some species which the original author studied personally, unless it can be definitely shown that he had some other species more particularly in mind.

(c) If the original genus has already been divided without designation of type, the type should be restricted by elimination, namely, by successively rejecting all the species which have already been transferred to other genera; the type is then selected from the species which remain.

If the genus contains both exotic and nonexotic species, from the standpoint of the original author, the type is to be selected from the nonexotic species.

(d) Select as type the species which is best described, or best figured, or best known.

DISCUSSION.—Every genus should have a single species, known as its "type," to serve as its standard of reference. This "type" should be designated by the author who proposes the genus. Unfortunately, many authors have failed to designate their "types," and because of this error of omission the nomenclature of some groups has become quite involved. In attempting to straighten out the technical names at present it is necessary to designate types for the older genera.

No existing code of nomenclature provides for all cases that arise, so that authors make supplemental rules for themselves. The rules which I personally adopt are the following:

1. **RULE.**—A genus proposed with a single original species takes that species as type. (Monotypical genera.)

2. **RULE.**—The type of a genus (containing, from the standpoint of the original author, both valid and doubtful species) must never be selected from any species which the original author of the genus clearly designated as a *species inquirenda* at the time of the publication of the generic name.

3. **RULE.**—When in the original publication of a genus one of the species is definitely designated as type this species should be accepted as type regardless of any other considerations. (Type by original designation.)

4a. **RULE.**—If, in the original publication of a genus, *typicus* or *typus* is used as a new specific name for one of the species, such use shall be construed as "type by original designation."

4b. RECOMMENDATION.—It is well to avoid the introduction of the names *typicus* or *typus* as new names for species or subspecies, since such names are always liable to result in later confusion.

5. RULE.—If a genus, without designated type, contains among its original species one possessing the generic name as its specific or subspecific name, either as valid name or synonym, that species or subspecies becomes ipso facto type of the genus. (Type by absolute tautonymy.)

6. RECOMMENDATION.—If a genus, without designated type, contains among its original species one possessing as specific or subspecific name, either as valid name or as synonym, a name which is virtually the same as the generic name, or of the same origin or same meaning, preference should be shown to that species in designating the type, unless such preference is strongly contraindicated by other factors. (Type by virtual tautonymy.)

7. RULE.—In case a generic name without designated type is proposed as a substitute for another generic name, with or without type, the type of either when established becomes ipso facto type of the other.

8. RULE.—If an author proposes a genus, without designating a type, and includes among the original species [i. e., the valid species from his standpoint] the determined type of an earlier genus, such type becomes ipso facto the type of the new genus. (Type by inclusion.)

9. RULE.—If a genus without a designated type contains types of two or more earlier genera, the type of the new genus is to be selected from the contained types (the case being the same as a genus with two or more species, according to the number of types in question), unless it can be shown that such procedure is directly contraindicated by the original author's intentions.

10. RULE.—If an author, in publishing a genus with more than one valid species, fails to designate or to indicate its type, any subsequent author may select the type, and such designation is not subject to change. (Type by subsequent designation.)

11. RULE.—Certain biological groups which have been distinctly proposed as collective groups, but not as systematic units of generic rank, may be treated for convenience as if they were genera, but they require no type species. Example: *Agamodistomum*.

12a. RULE.—The following species are excluded from consideration in selecting the types of genera:

(a) Species which were not included under the generic name at the time of its original publication.

(b) Species which were *species inquirendæ* from the standpoint of the author of the generic name at the time of its publication.

(c) Species which the author of the genus doubtfully referred to it.

(d) Species which have subsequently been selected to serve as types for other genera, unless this applies to all of the available species, in which case the last species so selected becomes the type of the original genus; or unless the species which the original author took as his type has been transferred, in which case the original author's intentions should be carried out. (Type by elimination.)

12b. RULE.—In case of Linnæan genera select as type the most common or the medicinal species. (Linnæan rule.)

12c. RECOMMENDATION.—The following species should be shown preference in selecting the type, unless such procedure is contraindicated by the original author's intentions or by practical considerations:

(a) If the genus contains both exotic and nonexotic species from the standpoint of the original author, the type should be selected from the nonexotic species.

(b) If some of the original species have later been classified in other genera, but not designated as their types, preference should be shown to the species still remaining in the original genus.

(c) All other things being equal, page precedence should obtain in selecting a type.

(d) Species based upon sexually mature specimens should take precedence over species based upon larval or immature forms.

(e) All other things being equal, show preference to a species which the author of a genus actually studied at or before the time he proposed the genus.

(f) Show preference to a species bearing the name *communis*, *vulgaris*, *medicinalis*, or *officinalis*.

(g) Show preference to the best described, best figured, best known, most easily obtainable species, or of which a type specimen can be obtained.

(h) Show preference to a species which belongs to a group containing as large a number of the species as possible.

(i) In parasitic genera, select if possible a species which occurs in man or in some food animal, or in some very common and widespread host.

Applying these rules to some of the generic names used by physicians, we arrive at the following results:

Genus TÆNIA Linnæus, 1758.

Type, *Tænia solium*. For generic synonymy see subgenera *Tænia* (p. 28) and *Tænia-rhynchus* (p. 29).

Subgenus TÆNIA Linnæus, 1758.

1758: *Tænia* Linnæus, 1758a, ^a 819-820; type by elimination *T. solium*; also designated type by several authors.

1777: *Tenia* Scopoli, 1777, 383; for *Tænia*, hence same type (not accessible, reference taken from Sherborn, 1902, 962).

1782: *Hydatigena* Goeze, 1782a, 42, 192; type by absolute tautonymy *Tænia hydatigena* Pallas, 1766, 413, confined by elimination and inclusion to *Hydra hydatula* Linnæus, 1767, equals *Cysticercus tenuicollis*.

1782: *Megocephalos* Goeze, 1782a, 42; only hence type species *Tænia vesicularis fasciolata*, equals *Cysticercus fasciolaris*.

1782: ? *Pseudoechinorhynchus* Goeze, 1782a, 41, 138-139; ? type *Ps. sp.* Goeze, 1782a, 138-139, equals ? *Cysticercus fasciolaris*.

1786: *Finna* Werner, 1786, 10; not used in Linnæan sense; refers to *Cysticercus cellulosa*.

1787: *Vesicaria* Müller, 1787, 49-53; includes *Hydatigena*, *Megocephalos*, *Multiceps*, 1782, and other forms; type by inclusion *Cysticercus tenuicollis*.

1788: *Vesicaria* Schrank, 1788a, 29-32; includes *Hydatigena*, *Megocephalos*, and *Multiceps*, 1782, renamed; type by inclusion and page precedence *V. orbicularis*, equals *Cysticercus tenuicollis*; also type by virtual tautonymy *Hydatigena vesicularis*, equals *Cysticercus tenuicollis*.

1790: *Hydatula* Abildgaard, 1790a, 33; type by absolute tautonymy *Hydra hydatula*.

1790: ? *Hæruca* Gmelin, 1790a, 3050; only hence type species *Hæruca muris* Gmelin, ? equals *Cysticercus fasciolaris*.

1797: *Hydatis* Blumenbach, 1797, 415; not accessible; apparently only hence type species *H. finna*, see Sherborn, 1902, 369, and Virey, 1798.

1800: *Alyselminthus* Zeder, 1800a, 221-302; *Tænia* renamed, hence same type.

1800: *Cysticercus* Zeder, 1800a, 303-307; *Hydatigena* renamed, hence same type.

^a The short bibliographic references used in this paper are taken from Stiles & Hassall, Index-Catalogue of Medical and Veterinary Zoology.

- 1803: *Halysis* Zeder, 1803a, 298–377; *Tænia* and *Alyselminthus* renamed, hence same type.
- 1805: *Cisticercus* Rudolphi, 1805, 40; for *Cysticercus*, hence same type.
- 1809: *Finna* Brera, 1809a, 153; type *muscularis*, equals *Cysticercus cellulosæ*.
- 1809: *Physchiosoma* Brera, 1809a, 130–149; type by inclusion *P. globosum* (Batsch, 1786), equals *Cysticercus tenuicollis*.
- 1810: *Goeziana* Rudolphi, 1810a, 277; refers to *Cysticercus cellulosæ*; doubtful whether it is used in generic sense.
- 1816: *Hydatigera* Lamarck, 1816, 153–154; type by inclusion and page precedence, *Cysticercus fasciolaris*.
- 1825: *Fischiosoma* delle Chiaje, 1825a, 24; for *Physchiosoma* Brera, 1809a.
- 1847: *Trachelocampylus* Fredault, 1847b, June, 310–311; only hence type species *Cysticercus cellulosæ*.
- 1850: *Arhynchotænia* Diesing, 1850a, 497–521; type by inclusion *Tænia solium*.
- 1858: *Acanthotrias* Weinland, 1858, 51, 65, 85; only hence type species and type by absolute tautonymy, *Cysticercus acanthotrias*.
- 1863: *Cystotænia* Leuckart, 1863, 223; type by inclusion *Tænia solium*.
- 1886: *Neotenia* Sodero, 1886, Oct., 657; type by inclusion and implication, *Cysticercus cellulosæ*.
- 1894: *Neotænia* Braun, 1894a, 1085; for *Neotenia*, hence same type.
- ?: *Cysticerkus* and *Cystizerkus* of various German authors; for *Cysticercus*, hence same type.

Subgenus TÆNIARHYNCHUS Weinland, 1858.

- 1823: *Pentastoma* Virey, 1823, 219–220 [not Rudolphi, 1819]; only hence type species *P. coarctata* n. sp. = *Tænia saginata*.
- 1858: *Tæniarhynchus* Weinland, 1858, 46, 51; only hence type species *Tænia medio-canellata* = *saginata*.

Genus ECHINOCOCCUS Rudolphi, 1801.

- 1782: *Hydatis* Goeze, 1782a, 192; very doubtful whether this is used in a generic sense.
- 1801: *Echinococcus* Rudolphi, 1801, 52–53; includes *Tænia multiceps* [type of *Multi-ceps*, 1782, and *Polycephalus*, 1800] and *Tænia visceralis socialis granulosa* Goeze, 1782, hence it is a deliberate renaming of a genus for which two names were already available, but Rudolphi definitely mentions “die körnigen Blasenwürmer” (namely, *granulosa*) as basis of *Echinococcus*, hence this is the type species; see also Rudolphi, 1802, 204.
- 1804: *Acephalocystis* Laennec, 1804, 132, 134–135; 1812, 96–123, 130–155, 170–173; type apparently *Echinococcus granulosis*, by inclusion.
- 1819: *Liococcus* Bremser, 1819a, 249; type *Echinococcus hominis*; genus not adopted by Bremser, 1819a.
- 1819: *Splanchnococcus* Bremser, 1819a, 249; *Echinococcus* renamed, hence same type.
- 1821: *Acephalocystus* Laennec of Merat, 1821, 229; for *Acephalocystis*, 1804, hence same type.
- 1829: *Acephalocistis* Cruveilhier, 1829a, 198; for *Acephalocystis*, 1804, hence same type.
- 1829: ?? *Acrostoma* Lesauvage, 1829, 433–438; only hence type species, *A. amnii*; probably pathological structure of amnion.
- 1844: ? *Astoma* Goodsir, 1844d, 282; only hence type species *A. acephalocystis* Goodsir.
- 1844: ? *Diskostoma* Goodsir in Gairdner, 1844a, 276; only hence type species *D. acephalocystis* Goodsir.
- 1844?: ? *Sphæridion* Goodsir; not accessible; see Gervais, 1847a, 92.
- 1858: *Echinococcifer* Weinland, 1858, 52, 61, 85; type *Tænia echinococcus*.
- 1894: ? *Discostoma* Braun, 1894a, 982; for *Diskostoma* Goodsir, 1844, hence same type.
- ?: *Echinokokkus* of various German authors, for *Echinococcus*, hence same type.

Genus *MONAS* Müller, 1773.

This genus was originally published with the diagnosis: “*Vermis inconspicuus, simplicissimus, pellucidus, punctiformis*,” to contain the three species *Monas termo*, *M. lens*, and *M. mica*. It is needless to say that with the technique of 1773 these species are not described with the minuteness that we expect to find in descriptions published at the present day, and if they are judged from the standards of 1905 instead of 1773, authors will doubtless admit that they may be applied to so many species that it is uncertain just which particular form Müller studied. If, however, this principle were applied generally to zoology and botany, we should be obliged to make a new start in nomenclature every few decades. The proper method to follow in a case of this kind is an historical study of the literature and synonymy, judging the subject from the successive standards as these improved, and accepting as correct the assertions of successive authors that they have recognized the older species, unless we are in a position to prove their assertions incorrect. The result of such a study is that early species are gradually narrowed down to closer limits until they become restricted to forms recognizable on basis of our present standards. In the case at hand the history of the three species in question, so far as literature is at my command, is as follows:

1. *Monas termo* Müller, 1773, 25-26. Ehrenberg, 1830a, 57, 81, etc., 1832c, 57, claims to have recognized this same species, adopting the name *Monas termo* Müller, but later authors (Dujardin, 1841a, 212; Diesing, 1850a, 16, 28) consider Ehrenberg's form distinct. Ehrenberg, 1832c, 70, also mentions a “*Bacterium? termo*.”

Dujardin, 1841a, 212, transferred “*Monas termo* Müller, non Ehrenberg” to *Bacterium* as *Bacterium termo* (Müller) Dujardin, and the species is retained here in Diesing, 1850a, 16.

Migula, 1897, 2, states that *Monas termo* Müller can with some certainty be viewed as belonging to the bacteria; Cohn (1872, 168) accepts *Bacterium termo* (as limited by Dujardin) as one of the two species of the genus *Bacterium*, as emended by him.

2. *Monas lens* Müller, 1773, 26-27. Retained in *Monas* by Dujardin, 1841a, 280; placed in subgenus *Mastichemonas* by Diesing, 1850a, 32. Migula, 1897, 2, thinks this species belongs to the bacteria.

3. *Monas mica* Müller, 1773, 27. Retained in *Eumonas* (typical subgenus of *Monas*) by Diesing, 1850a, 25. This species is thus seen to be type of the genus *Monas*, by elimination, and as limited by Diesing, 1850a.

Genus *BACTERIUM* Ehrenberg, 1828.

[Not *Bactiria* Fisch., 1811, echinoderm; not *Bacteria* Latreille, 1825, orthopteron; not *Bacteria* for *Bactiria*, 1811.]

1828: *Bacterium* Ehrenberg in Hemprich & Ehrenberg, 1828; Ehrenberg, 1830a, 58.

The use of *Bactiria*, 1811, and *Bacteria*, 1825, does not necessarily invalidate *Bacterium*, 1828.

The genus *Bacterium* was first proposed by Ehrenberg in a paper presented before the Academy of Science, Berlin, Germany, on Janu-

ary 10, 1828, but this was not published until 1829 or possibly until 1830. In the meantime Hemprich & Ehrenberg's (1828a) *Symbolæ physicae*, v. 4, appeared, in which *Bacterium* is also published as a new genus. According to the zoological code, it dates from this (1828) paper, since this is its first publication. The original diagnosis reads as follows:

Bacterium, Novum Genus, Familia *Vibrioniorum*.

Charater Generis: Corpus polygastricum? anenterum? nudum, oblongum, fusiforme aut filiforme, rectum, monomorphum (contractione nunquam dilatatum), parum flexile (nec aperte undatum), transverse in multas parte sponte dividuum.

B. triloculare nov. spec.: distincte triloculare s. triarticulatum, subfusiforme, hyalinum. Phytozoa Tab. II. Libya fig. 6.

Animalculum $\frac{1}{300}$ lineæ longum, corpore tereti. Articuli s. septa interna divisionem instantem multiplicem transversam indicare videntur. Mobile sed pigrum animalculum.

In Oasi Iovis Hammonis Siwæ observatum, præterea nullibi.

Bacterii Generis physiologia hucusque obscura. Cibo colorato ventriculos replere hæ formæ respuunt ideoque ad Polygastrica non nisi dubitanter et interim collocantur.

Bacterium simplex vide *Monas simplex*.

—— *scintillans* vide *Monas scintillans*.

Later in the paper, reference is made to "6 species," but these do not appear to have been named.

In his next paper, Ehrenberg (1829 or 1830a, 15) mentioned briefly *Bacterium triloculare*, *B. simplex*, and *B. scintillans*, but as the two latter species were eliminated by him from *Bacterium* in 1828, *B. triloculare* remains as type of the genus.

In a third paper presented to the Berlin Academy by Ehrenberg on March 4 and 18, and printed on August 13, 1830, Ehrenberg (1830a, 58) again referred to *Bacterium* as a new genus with the following diagnosis:

Corpore oblongo, fusiformi aut filiformi (tereti aut triquetro nec quadrangulo) aperte undatim non flexili, nec spirali.

He states that there are 11 species in this genus and later in the paper he mentions *Bacterium tremulans*, "*B. monas?*" *B. cylindricum*, *B. deses*, *B. enchelys*, *B. fuscum*, and *B. punctum*.

In a paper presented to the Academy in 1831, Ehrenberg (1832, p. 59) eliminates *B. cylindricum* and *B. deses* to *Monas*; on page 60 *Bacterium simplex* Hemprich & Ehrenberg is given as *Monas simplex*, and *Bacterium scintillans* as *Monas scintillans*; under the genus *Bacterium* he gives the following:

Bacterium E., Gliederstäbchen.

+) deutliche Gliederung.

1. *B. articulatum* E., Perlenschnur-Gliederstäbchen, Längendurchmesser $1/192'''$. Körper farblos, etwas spindelförmig, wenig biegsam, mit mehreren deutlichen Abtheilungen (Spuren der Selbsttheilung). Bewegung zitternd. Berlin.

2. *B. triloculare* H. & E., dreifächriges Gliederstäbchen, Längendurchm. $1/300'''$. Körper etwas spindelförmig, farblos, mit drei Abtheilungen. Afrika.

++) undeutliche Gliederung. [Here are given four species as doubtful, namely, "*B. ?enchelys* E.," "*B. ?punctum* E.," "*B. ?tremulans* E.," and "*B. ?termo* E."]

In his noted monograph Ehrenberg (1838a, 75-77) again cites *Bacterium*. He states that—

ganz sicher ist nur eine Art der Gattung. Nur bei *B. triloculare* ist thierische wirkliche Organisation beobachtet, indem sich ein wirbelnder Rüssel erkennen liess. Ausserdem ist körnige Trübung und die Selbsttheilung erkannt. Nur die, freilich sehr kräftige, offenbar freie, Bewegung ist ein allen Formen gemeinsamer thierischer Character. * * * *Bacterium triloculare* ist zuerst in der Oase des Jupiter Ammon in libyschen Africa, dann auch bei Berlin beobachtet, *B. enchelys* und *punctum* sind bisher nur in Petersburg gesehen.

B. triloculare, the type of the genus, was first found in 1820 in swamp water in Africa. Later (1831) Ehrenberg found a similar form near Berlin, which he published as *B. articulatum*. In 1833 Ehrenberg again found this form in a glass of stagnant water in his room in Berlin, and he considered *B. triloculare* and *B. articulatum* as identical. He further observed a terminal flagellum on the organism ("einen einfachen fadenartigen kurzen Rüssel;") this was one-third to one-half as long as the body; "die Bewegung der Thierchen war zitternd und um die Längsaxe langsam wälzend." As doubtful species, Ehrenberg gives *B. enchelys* and *B. punctum*.

As Ehrenberg, the author of both *Bacterium triloculare* and *B. articulatum*, concluded that these two supposedly distinct forms were in reality specifically identical, this conclusion should be accepted as correct until proved to be incorrect, and as he describes his type as possessing a terminal flagellum, *Bacterium* should be taken to possess this character.

It is unnecessary to follow the genus further, in so far as a determination of the type species is concerned, but it is interesting to note its later history.

Dujardin (1841a, 212-216) retains the genus *Bacterium* with the following diagnosis:

Corps filiforme, roide, devenant plus ou moins distinctement articulé par suite d'une division spontanée imparfaite. Mouvement vacillant non ondulatoire.

He cites the following species:

1. *B. termo* (Müller); with the synonyms: *Monas termo* Müller, not Ehrenberg; *Vibrio lineola* Ehrenberg; this was not one of the original species.
 2. *B. catenula* new species.
 3. *B. punctum* Ehrenberg; synonyms: *Monas punctum?* Müller; *Melanella punctum?* Bory; *Bacterium punctum?* Ehrenberg.
- Bacterium triloculare* or *B. articulatum* and *B. ?enchelys*.

Diesing (1850a, 14-16) describes *Bacterium* as—

Corpus nudum, lorica destitutum haud mutabile, cylindricum subovatum aut subglobosum, partitione imperfecta uniseriali, multiplici, transversa in syntherium lineare, moniliforme, rigidulum, rectum, hyalinum accrescens. Os * * * Flagellum in articulo primo terminale simplex. Ocellus nullus.

1. *B. triloculare* Hemprich & Ehrenberg; syn. *B. articulatum* Ehrenberg.
2. *B. enchelys* Ehrenberg; sp. inquirenda.
3. *B. punctum* Ehrenberg; sp. inquirenda; syns. *Monas punctum* Müller?; *Melanella monadina* Bory, 1824; *Bacterium punctum* Ehrenberg; *Bacterium?* *punctum* Ehrenberg, and Dujardin.
4. *Bacterium termo* (Müller) Dujardin; sp. inquirenda; syn. *Monas termo* Müller.

Cohn (1872, 168) in his emended *Bacterium* cites two species, namely: *B. termo* Ehrenberg, 1830, Dujardin, 1841; and *B. lineola* (Müller). As neither of these species was among the original species of the genus (1828), and as Ehrenberg himself, as author of the genus, cited (1832a, 59) "*B.? termo*" with reserve, it will be seen that Cohn has used the genus in a sense not altogether in harmony with its first publication (namely, he eliminated the type of the genus).

Migula (1897, 4) states that *Bacterium triloculare*, *B. enchelys*, and *B. punctum* of Ehrenberg are no longer recognizable. As diagnosis of the genus he (1900, 280) gives the following:

Kürze oder lange cylindrische Zellen, zuweilen Fäden von nicht unbeträchtlicher Länge bildend, *ohne* Geisseln. Endosporenbildung ist bei vielen Arten bekannt, bei anderen scheint sie vollkommen zu fehlen, bei vielen jedoch dürften sie noch bei passenden Bedingungen nachzuweisen sein.

It will be thus seen that *Bacterium* Ehrenberg as used by Migula is not in harmony with Ehrenberg's description of his type, namely, a flagellated form.

If bacteriologists continue to use *Bacterium* in the sense used by Migula, the question does not concern the zoologists and does not come under the zoological code. Our duty with the genus ceases with the date that *Bacterium* was eliminated from zoology. The zoological code provides, however, that the generic name preserves its nomenclatural status and that we can not use *Bacterium* for any other later genus or supposed genus in zoology. Should the time come that *Bacterium* is transferred again to the protozoa, it should, according to the zoological code, be judged upon the basis of its type, *Bacterium triloculare*.

Species BACTERIUM ARTICULATUM Kern, 1897.

Migula gives *Bacterium articulatum* Kern, 1897, as a valid species of *Bacterium*, but attention may be called to the fact that Ehrenberg, 1832c, 69, reports a *Bacterium articulatum*. Kern's species can not retain this name unless it is claimed that it is identical with Ehrenberg's form, in which case it should be attributed to Ehrenberg. Ehrenberg (1838a) cites *B. articulatum* Ehrenberg as a synonym of *B. triloculare* Hemprich & Ehrenberg.

Genus SPIRILLUM Ehrenberg, 1830.

[Not *Spirilla* Humph., 1797, mollusk; not *Spirillum* Oken, 1815, worm; not *Spirillus* Schlüt, 1838, mollusk.]

1830: *Spirillum* Ehrenberg, 1830a, 58; type by absolute tautonymy, *Vibrio spirillum*.

This genus was originally published with the diagnosis, “corpore filiforme rigido spirali,” and contained two species, namely:

1. *Spirillum volutans* Ehrenberg, equals *Vibrio spirillum* Müller, renamed.
2. *Spirillum undula* (Müller, 1773), namely, *Vibrio undula*.

Judged from the zoological point of view, *Vibrio spirillum* is the type species by absolute tautonymy. but the zoological name *Spirillum*, 1830, was a stillborn homonym, having been used by Oken, 1815, for a genus of polychæte worms. It is not the function of the zoological code to determine the names in bacteriology, but it is undoubtedly not the most wise or farseeing policy for either zoologists or botanists (including bacteriologists) to accept unnecessarily a generic name for organisms so near the border line when that name is a homonym in either zoology or botany; should further investigations again bring bacteriology into zoology, the generic names would come under the zoological code, and in this case *Spirillum*, 1830, would be rejected. If *Spirillum* is retained in bacteriology, consistency calls for the rejection of the name *Spirillum volutans* Ehrenberg in favor of *Spirillum spirillum* (Müller).

Genus SPIRODISCUS Ehrenberg, 1830a.

[Not *Spirodiscus* Stein, 1850, mollusk.]

Only, hence type species *Spirodiscus fulvus* Ehrenberg, 1830a, 85.

Genus SPIROCHÆTA Ehrenberg, 1834.

[Not *Spirochæta* Sars., 1856, worm.]

1834: *Spirochæta* Ehrenberg, 1834a, 169. Only, hence type species *Spirochæta plicatilis* Ehrenberg, 1834; type locality, Berlin, Germany, in water.

1841: *Spirochæta* Dujardin, 1841a, 225; for *Spirochæta*.

1872: *Spirochæte* Cohn, 1872, 180; for *Spirochæta*.

This genus originally contained only one species; hence there can be no question as to the type. This species figures in literature as *Spirochæta plicatilis*, *Spirillum plicatile*, and *Spirulina plicatilis*. The generic name preoccupies *Spirochæta* Sars., 1856, worm.

Since Ehrenberg described *Spirochæta* several new species have been added to the genus. Should future investigations result in a division of the group the name *Spirochæta* must be preserved for the subdivision containing *S. plicatilis*.

Genus BACILLUS Cohn, 1872.

[Not *Bacillus* Latreille, 1825, orthopteron.]

This genus was proposed by Cohn as a genus of plants, namely, after the bacteria had been eliminated from zoology; accordingly the name is not influenced by the existence of *Bacillus* Latreille, 1825. If, however, later investigations should again transfer this genus to the animals, the name *Bacillus* Cohn should be rejected by zoologists because of *Bacillus* Latreille, 1825.

Cohn's genus originally contained three species, as follows:

1. *Bacillus subtilis* (Ehrenberg, 1833) Cohn, 1872; Cohn records *Vibrio subtilis* Ehrenberg as synonym.
2. *Bacillus anthracis* Cohn, 1872; not examined by Cohn. To *Bacterium* by later authors.
3. *Bacillus ulna* Cohn, 1872; retained in *Bacillus* by Migula.

Cohn (1872, 178) mentions *Vibrio bacillus* in his discussion of *Bacillus*, but it is not clear that he definitely includes *V. bacillus* in the genus. This does not, therefore, appear to be a clear case of type by absolute tautonymy. If this case were ruled upon by page precedence, *Bacillus subtilis* would be the type. If preference were shown to the medicinal species (Linnaean rule) *Bacillus anthracis* would be taken as type. This ruling is, however, contraindicated by two factors, namely: *B. anthracis* was not examined by Cohn, and it has been eliminated from *Bacillus*. It would be better to take a species examined by Cohn and one not since eliminated. Were I ruling on this case as a zoological genus, I should accept *B. subtilis* as type of *Bacillus*.

Art. 31. The division of a species into two or more restricted species is subject to the same rules as the division of a genus. But a specific name which undoubtedly rests upon an error of identification can not be retained for the misdetermined species even if the species in question are afterwards placed in different genera. Example: *Tænia pectinata* Goeze, 1782 = *Cittotænia pectinata* (Goeze), but the species erroneously determined by Zeder, 1800, as "*Tænia pectinata* Goeze" = *Andrya rhopalocephala* (Riehm); the latter species does not take the name *Andrya pectinata* (Zeder).

DISCUSSION.—The species *Tænia solium*, 1758, included both *T. solium* and *T. saginata* of the present day. Bloch (1782a) definitely cited *T. solium* as an armed species; Goeze (1782a) showed that two forms were present, but he fell into error in renaming both species; again the two species were confused, but Virey (1823) named *Pentastoma coarctata* (which corresponds to the unarmed species) as a new form; later authors confined *T. solium* to the armed species. The history of the species calls for the retention of *T. solium* for one of the species, and the name has been quite generally applied to the

armed form. Goeze's name *saginata* seems to be the oldest available name for the unarmed form.

The question might be raised as to whether Gmelin's (1790) use of *Tænia cellulosæ* for the larval stage of the armed form should not be accepted as reversing the names, but this point may be met with the statement that Bloch (1782) definitely stated that *Tænia solium* is an armed species.

The synonymy, so far as I have followed it, is as follows:

Species **TÆNIA SOLIUM** Linnæus, 1758.

STROBILA STAGE.

- 1758: *Tænia solium* Linnæus, 1758a, 819-820, after elimination of *T. saginata* and *T. marginata*; included: *Tænia osculis marginalibus solitariis* Dubois, 1848a, 13-17, fig. 1; *Tænia articulata teres* Linnæus, 1746, 1267; *Lumbricus latus* Tyson, 1683, pl. 1, pl. 2, figs. 2, 6, 10; *Solium* Andry, lumb., f. 5; Bewerw. thes. 202, t. 202, f. 3; *Vermis cucurbitinus* Plater, 1609, 993; *Lumbricus latus* Coulet. monogr.
- 1766: *T. cucurbitina* Pallas, 1766, 405-407; not accessible; *T. solium*, 1758, renamed.
- 1782: *T. cucurbitina* Bloch, 1782a, 20-23; armed form, not available, because of *T. cucurbitina*, 1766, which contained both species.
- 1782: *T. cucurbitina pellucida* Goeze, 1782a, 42.
- 1782: *T. cucurbitina, plana, pellucida*, Goeze, 1782a, 278, 282-286, pl. 21, figs. 5, 9, 10.
- 1782: ? *T. vulgaris* Werner, 1782, 49-54, pl. 2, figs. 47-57; not Linnæus, 1758.
- 1784: *T. solitaria* Leske, 1784 or 1785, not accessible; see Seeger, 1852, 11, as syn. of *T. solium*.
- 1786: ? *T. dentata* Batsch, 1786a, 184-187, figs. 110-113 (not Nicolai, 1830); *T. vulgaris* Werner, 1782, renamed.
- 1790: *T. plana pellucida* Goeze, 1782a, of Gmelin, 1790a, 3065.
- 1802: *Tenia armata umana* Brera, 1802a, 21-24, pl. 1, figs. 1-3, 6, 8, 10, 11.
- 1803: *Halysis solium* (Linnæus, 1758a), Zeder, 1803a, 359-361.
- 1808: *Tænia armata hominis* Brera, 1808a, 64-80, pl. 1, figs. 1-14, 17-22.
- 1810: *T. humana armata* Rudolphi, 1810a, 161; in synonymy.
- 1833: ? *T. fenestrata* Chiaje, 1833a, 20, pl. 3, fig. 2.
- 1852: *T. solium* Linnæus, 1758, partim Küchenmeister, 1852f, 101-103.
- 1855: *T. hamoloculata* Küchenmeister, 1855a, 64; *T. solium* Linnæus, 1758a, partim Küchenmeister, 1852, renamed.
- 1861: *T. turbinata* Kœberlé, 1861a, 329; based on *Cysticercus turbinatus*.
- 1861: *T. melanocephala* Kœberlé, 1861a, 329, based on *Cysticercus melanocephalus*.
- 1861: *Tenia solium* (Linnæus, 1758) Beneden, 1861a, 144-146.
- 1861: *T. cucurbitina* Goeze of Beneden, 1861a, 144, in synonymy.
- 1863: *Tænia* [(*Cystotaenia*)] *solium* Linnæus of Leuckart, 1863, 223, 225.
- 1863: *T. (Cysticercus) acanthotrias* (Weinland, 1858) Leuckart, 1863, 310-312, figs. 86-87.
- 1874: *T. tenella* Cobbold, 1874v, 888 (not Pallas, 1781).
- 1876: *T. solium fenestrata* Colin, 1876a, 323, 324, fig. 1; Maggiora, 1891, 147.
- 1885: *T. solium minor* Guzzardi Asmundo, 1885a, 577-582, figs. 1-15.
- 1885: *Tenia tenella* (Cobbold, 1874) Guzzardi Asmundo, 1885a, 579-580.
- 1885: *Tænia scalariforme* Notta, 1885, 673-675; *T. solium fenestrata* Colin, renamed.
- 1885: *T. solium scalariforme* Notta, 1885, 675; same as *T. scalariforme*.
- 1894: *T. officinalis* Bos, 1894a, 234, fig. 136; for *Tænia solium*.
- 1894: *T. tenelal* Pepper, 1894, 871; misprint for *T. tenella* Cobbold, 1874v.

CYSTIC STAGE.

- 1783: *Vesicaria lobata* Fabricius, 1783, 287–295, figs. 1–5; see Diesing, 1850a, 486.
- 1786: *Finna* Werner, 1786, 10; not in generic sense.
- 1786: *Finna humana* Fischer in Werner & Fischer, 1786, 50, pl. 1, figs. 1–8; in man; not binomial.
- 1788: *Tænia hydatigena* Fischer, 1788b, 65–77, pl. 5, figs. 1–9; in carne suis; not consistently binomial.
- 1789: *T. hydatigena* Fischer, 1789a, 25; in man; not binomial.
- 1789: *Hydatis piriformis* Fischer, 1789a, 42, figs. 1–5; not as binomial.
- 1790: *Tænia cellulosæ* Gmelin, 1790a, 3059; based on Werner, 1786, 10, pl. 1, figs. 1–8; in man.
- 1790: *T. finna* Gmelin, 1790a, 3063–3064; based on Fischer, 1788b, 65, pl. 5; in hogs.
- 1793: *Vesicaria hygroma humana* Schrank, 1793, 137; not accessible; see Diesing, 1850a, 486.
- 1793: *V. finna suilla* Schrank, 1793, 137; not accessible; see Diesing, 1850a, 486.
- 1793: *Tænia albopunctata* Treutler, 1793, 1–9, pl. 2, figs. 1–2; in man; Jördens, 1802a, 61–62, pl. 6, figs. 1–2; Lænnec, 1804, and 1812, 69–75.
- 1793: *T. pyriformis* Treutler, 1793, 8.
- 1797: *Hydatis finna* (Gmelin, 1790) Blumenbach, 1797, 415; not accessible; 1816a, 12–13.
- 1798: *H. cellulosæ* (Gmelin, 1790a) Virey, 1798, 435.
- ?: *H. humana* Blumenbach, —?—; not accessible; see delle Chiaje, 1825a, 24–25.
- 1802: *Tænia muscularis* Jördens, 1802a, 57–59, pl. 5, figs. 12–16; *Finna humana* Fischer, 1786, named binomially.
- 1802: *T. piriformis* Jördens, 1802a, 59–61, pl. 5, figs. 17–21; *Tænia hydatigena* Fischer, 1789a, p. 25, figs. 1–5, renamed.
- 1802: *T. hydatigena anomala* Steinbuch, 1802; not accessible; see Diesing, 1850a, 486.
- 1803: *T. collulosa* Treutler of Zeder, 1803a, 407; in synonymy.
- 1803: *Cysticercus albopunctatus* (Treutler, 1793) Zeder, 1803a, 421.
- 1803: *C. pyriformis* (Treutler, 1793) Zeder, 1803a, 414.
- 1803: *C. finna* (Gmelin, 1790a) Zeder, 1803a, 407–409.
- 1804: *C. finnus* (Gmelin, 1790a) Lænnec, 1804, 133; 1812, 46–57, 158.
- 1804: *C. dicystus* Lænnec, 1804, 133, n. sp., in man; 1812, 61–69, 162.
- 1804: *C. fischerianus* Lænnec, 1804, 133; 1812, 57–61, 161; *Hydatis piriformis* Fischer, 1789, renamed.
- 1805: *Cisticercus finna* (Gmelin, 1790a) Rudolphi, 1805, v. 2, 40.
- 1808: *Cysticercus cellulosæ* (Gmelin, 1790a) Rudolphi, 1808a, 116–118.
- 1809: *Fischiosoma pyriforme* (Treutler, 1793) Brera, 1809a, 138; probably not intended for Latin; see *Physchiosoma pyriforme*.
- 1809: *Physchiosoma pyriforme* (Treutler, 1793) Brera, 1809a, 138–140.
- 1809: “*Finna cisticercus* Zeder” of Brera, 1809a, 154; in synonymy.
- 1809: *Finna muscularis* (Jördens, 1802) Brera, 1809a, 153–159, pl. 2, figs. 11–13; pl. 3, figs. 6–10.
- 1810: ? *Cysticercus canis* Rudolphi, 1810a, 234–235; Kœberlé, 1861a, 183.
- 1812: *Tænia cellulosa* (Gmelin, 1790a) Lænnec, 1812, 158, in synonymy.
- 1816: *H. finna* (Gmelin, 1790a) Blumenbach, 1816a, 12; probably 1807a; from swine; 1825a, 243; 1827a, 1 pl., 2 figs.
- 1816: *C. cellulosæ* Lamarck, 1816, 154; for *C. cellulosæ*.
- 1816: *Hydatigera cellulosæ* Lamarck, 1816, 154.
- 1825: *Tænia hydatigena suilla* Fischer of delle Chiaje, 1825a, 24–25; in synonymy.
- 1825: *Cysticercus cellulosa* (Gmelin, 1790) Cuvier, 1825a, 90.
- 1825: *Vesicaria finna* Schrank (not accessible) of delle Chiaje, 1825a, 24–25.
- 1825: *V. hygrometra* Schrank (not accessible) of delle Chiaje, 1825a, 24–25.

- 1825: "*Finna cysticercus* Zeder" of delle Chiaje, 1825a, 24, in synonymy.
 1825: *Hydatis lanceolata* Lam. (not accessible) of delle Chiaje, 1825a, 24–25.
 1837: *Tænia albopuocata* Tschudi, 1837, 54; misprint for *albopunctata*.
 1840: ? *T. hydatigena* in letter to Creplin, 1840a, 150.
 1847: *Trachelocampylus* Fredault, 1847b, June, 310–311.
 1850: *Tænia albopunctata hominis* Treutler of Diesing, 1850a, 486; in synonymy.
 1850: *Vesicaria lobata suilla* Fabricius, 1783, of Diesing, 1850a, 486; in synonymy.
 1850: *Vermis vesicularis* Brera of Diesing, 1850a, 486; in synonymy.
 1850: *Cysticercus cellulosa* (Gmelin, 1790) Diesing, 1850a, 486–488.
 1850: ? *C. vesicæ hominis* Creplin, 1840, of Diesing, 1850a, 492.
 1850: *Hydatigena cellulosa* Lamarck of Diesing, 1850a, 487; in synonymy.
 1850: *Tænia cellulosa* Gmelin of Diesing, 1850a, 486; in synonymy.
 1858: *Acanthotrias* Weinland, 1858, 51, 65, 85; type *C. acanthotrias*.
 1858: *Cysticercus acanthotrias* Weinland, 1858, 64, 67, 85, figs. 11–12; n. sp., in man.
 1860: ? *C. vesicæ* Creplin, 1840, of Moquin-Tandon, 1860, 369.
 1861: *Tænia hydatigena eremita* Werner of Kœberlé, 1861a, 183; in man.
 1861: *T. hydatigena* Kœberlé, 1861a, 183; of pork.
 1861: *Cysticercus solium* (Linnæus, 1758a) Kœberlé, 1861a, 183, 328, 329, 334.
 1861: *C. turbinatus* Kœberlé, 1861a, 219, 263–264, 334; includes *trachelocampyle*.
 1861: *C. melanocephalus* Kœberlé, 1861a, 183, 264–265, 328, 329, 334, pl. 2, fig. 1; n. sp., in man.
 —?: *C. multilocularis* Küchenmeister; not accessible.
 1869: *C. suis* Cobbold, 1869a, 30; *C. cellulosa*, renamed.
 1874: *C. racemosus* Heller, 1874a, 334; in brain of man.
 1874: *C. botryoides* Heller, 1874a, 334 (not Reinitz, 1885); = *C. racemosus*.
 1886: *Neotenia* Sodero, 1886, 650–662, figs. 1–10; *C. cellulosa*, renamed.
 1894: *Neotænia* Braun, 1894a, 1085; for *Neotenia* Sodero, 1886.
 1896: *Cysticercus cellulosa* (Gmelin, 1790a) Schneidemühl, 1896, 274, 275, 276–277; for *Cysticercus cellulosa*.
 1898: *Tænia hydatigera* Fischer, 1788, of Stiles, 1898, 89; misprint for *T. hydatigena*.

Species TÆNIA SAGINATA Goeze, 1782.

STROBILA STAGE.

- 1758: *Tænia solium* Linnæus, 1758a, 819–820, pro parte.
 1766: *T. cucurbitina* Pallas, 1766, 405–407, pro parte; not accessible.
 1782: *T. cucurbitina saginata* Goeze, 1782a, 42.
 1782: *T. cucurbitina grandis saginata* Goeze, 1782a, 278.
 1782: ?*T. vulgaris* Werner, 1782, 49–54, pl. 3, figs. 47–57.
 1785: ?*T. solitaria* Leske, 1785, pro parte; not accessible.
 1786: ?*T. dentata* Batsch, 1786a, 184–187, figs. 110–113; *T. vulgaris* Werner, 1782, renamed.
 1790: *T. grandis* Gmelin, 1790a, 3065; in synonymy.
 1803: *Halysis solium* (Linnæus, 1758a) Zeder, 1803a, 359–361, pro parte.
 1823: *Pentastoma coarctata* Virey, 1823, 219–220.
 1830: *Tænia dentata* Nicolai, 1830, 464 (not Batsch, 1786); not accessible; see Diesing, 1863a, 366.
 1833: ?*T. fenestrata* delle Chiaje, 1833a, 20, pl. 3, fig. 2; based on de Cazeles, 1768a, 26–43.
 1847: *T. lata* Pruner, 1847, 245–246; not Linnæus, 1758a; see Diesing, 1863a, 367, and Blanchard, 1886a, 315.
 1847: *T. tenella* Pruner, 1847, 245; not Pallas, 1781; see Diesing, 1853a, 369.

- 1847: *Bothriocephalus tropicus* Schmidtmüller, 1847, 602–603.
 1852: *Tænia mediocanellata* Küchenmeister, 1852f, 101–103.
 1852: *T. mediocanellata hominis* Küchenmeister, 1852f, 101–103.
 1852: *T. zittaviensis* Küchenmeister, 1852f, 101–103.
 1854: *T. solium mediocanellata* Diesing, 1854b; 1854c, p. 51.
 1855: *T. vom Cap der guten Hoffnung* Küchenmeister, 1855a, 93–95.
 1858: *T. [Tæniarhynchus] mediocanellata* Küchenmeister of Weinland, 1858, 46, 51.
 1858: *T. solium abietina* Weinland, 1858, 43–45, 84.
 1860: *T. inermis* Moquin-Tandon, 1860, 359, 425; Laboulbène, 1876, 189; not Brera, 1803a.
 1860: *T. tropica* (Schmidtmüller, 1847) Moquin-Tandon, 1860, 360.
 1860: “*T. medicancellata* of several authors,” Moquin-Tandon, 1860, 359.
 1860: *T. capensis* Moquin-Tandon, 1860, 359.
 1861: *Tæniarhynchus mediocanellatus* (Küchenmeister, 1852) Weinland, 1861, 18; see Diesing, 1863a, 368.
 1861: *Tænia megaloon* Weinland, 1861, 118–120, figs.; not accessible.
 1863: *T. [(Cystotænia)] mediocanellata* Küchenmeister of Leuckart, 1863, 285.
 1866: *T. lophosoma* Cobbold, 1866p, 438–439; 1866, 52–54.
 1867: *T. saginata* Goeze of Leuckart, 1867, 284.
 1873: *T. abietina* Weinland, 1858, of Davaine, 1873a, 572.
 1876: ? *T. fusa* Colin, 1876a, 323.
 1876: ? *T. continua* Colin, 1876a, 323, fig. 2.
 1876: ? *T. solium fusa* Colin, 1876a, 324, fig. 2.
 1876: ? *T. solium continua* Colin, 1876a, 324, fig. 2.
 1877: *T. nigra* Davaine, 1877a, 1000; based upon Laboulbène’s observation.
 1883: *T. algérien* Redon, 1883, 182, 183.
 1885: *Tænia abietina* (Weinland) Guzzardi Asmundo, 1885a, 580.
 1885: *T. mediocanellata* (Küchenmeister) Guzzardi Asmundo, 1885a, 580.
 1885: *Tænia mummificata* Guzzardi Asmundo, 1885a, 579 [“*saginata* or *solium*”].
 1885: *Tænia cosidetta mummificata* Guzzardi Asmundo, 1885a, 579 [*solium* or *saginata*].
 1886: *Tænia saginata abietina* Weinland of Leuckart (Hoyle), 1886, 479, fig. 272.
 1886: *Tænia seghettata* Bergonzini, 1886a, 309; not as Latin name.
 1891: *Tænia inermis fenestrata* Maggiora, 1891, 145–151.
 1891: *T. perforata* Maggiora, 1891, 147; based on Leuckart, 1880, 579, fig. 263.
 1894: *T. algeriana* Pepper, 1894, 871; for *T. algérien* Redon, 1883.
 1894: *T. algeriensis* Braun, 1894a, 1074; for *T. algérien* Redon, 1883.

CYSTIC STAGE.

- 1863: *Cysticercus tæniæ mediocanellatæ* Leuckart, 1863, 408.
 1866: *C. bovis* Cobbold, 1866a, 77; 1866r, 462.
 1877: *C. inermis* Davaine, 1877a, xlv.
 1880: *C. tæniæ saginatæ* Leuckart, 1880, 586; probably earlier.
 1896: *Cysticercus bovis* (Cobbold, 1866) Schneidemühl, 1896, 278.
 1896: *C. tæniæ saginatæ* (Leuckart) Schneidemühl, 1896, 278–279.

Genus DIPYLIDIUM Leuckart, 1863.

- 1863: *Dipylidium* Leuckart, 1863, 400; type *Tænia “elliptica”* Batsch = *canina* Linnæus, 1758.
 1858: *Alyselminthus* Weinland, 1858, 53; type *T. cucumerina* = *T. canina* Linnæus, 1758; [not *Alyselminthus* Zeder, 1800 = *Tænia*, renamed, hence type *T. solium*.]
 1882: *Cercocystis* Villot, 1882, 8–9; type *Cercocystis trichodectis* equals *Dipylidium caninum*.
 1884: *Microtænia* Sedgwick, 1884, 336; type by inclusion, *Dipylidium caninum*.

Species DIPYLIDIUM CANINUM (Linnæus, 1758).

STROBILA STAGE.

- 1758: *Tænia canina* Linnæus, 1758a, 820; included: *Tænia* osculis marginalibus oppositis Dubois, 1748a, 20–21, fig. 4; Ruysch., obs. 84; Act. Stockh. 1747, t. 5, f. a.
- 1781: *T. moniliformis* Pallas, 1781; not accessible; not Batsch, 1786.
- 1782: *T. cucumerina* Bloch, 1782a, 17, pl. 5, figs. 6–7; from dog, with *T. canina* Linnæus as possible synonym.
- 1782: *T. cateniformis* Goeze, 1782a, 42, 306–337 [includes *T. canina* Linn. as synonym, and also other forms; is best construed as a renaming of *T. canina*, 1758.]
- 1782: *T. elliptica* Goeze, 1782a, 312, equals *T. canina* Linnæus, 1758, renamed.
- 1786: *T. ellyptica* Batsch, 1786a, 129–133, figs. 7, 8, 24–26, 57, 65, 121; for *T. canina* Linnæus, 1758, and *T. elliptica* Goeze, 1782; [dog and cat].
- 1788: *T. moniliformis* Schrank, 1788a, 34 [not Batsch, 1786]; based on Goeze 1782a, pl. 22b, figs. 13–22 [from cat].
- 1790: *T. cateniformis canina* Linnæus, 1758, in Gmelin, 1790a, 3066.
- 1790: *T. cateniformis felis* Gmelin, 1790a, 3067; based on Goeze, 1782a, 315, pl. 22b, figs. 13–22; from cats.
- 1800: *Alyselminthus ellypticus* (Batsch, 1786a) Zeder, 1800a, 290.
- 1803: *Halysis ellyptica* (Batsch, 1786a) Zeder, 1803c, 361–363.
- 1861: *Tenia canina* Beneden, 1861a, 157–158, pl. 21, figs. 1–14.
- 1861: *T. cucumerina* (Bloch, 1782a) Beneden, 1861a, 157; in synonymy.
- 1863: *Tænia* [(*Dipylidium*)] *cucumerina* of Leuckart, 1863, 400.
- 1882: *Cryptocystis trichodectis* Villot, 1882, 8–9.
- 1893: *Dipylidium caninum* (Linnæus, 1758a) Railliet, 1893a, 284–290, figs. 181–189.

Genus DIBOTHRIOCEPHALUS Lühe, 1899.

Species DIBOTHRIOCEPHALUS LATUS (Linnæus, 1758) Lühe, 1899.

- 1758a: *Tænia lata* Linnæus, 1758a, 820, to include: *Tænia* osculis lateralibus solitariis Dubois, 1748a, 19–20, fig. 3.
- 1758: *T. vulgaris* Linnæus, 1758a, 820, to include: *Tænia* osculis lateralibus geminis Dubois, 1748a, 17–18, fig. 2; *Tænia articulata plana* Linnæus, 1746a, 363; *Lumbricus latus s. intestinorum* Plater, 1609, 992; “*Tænia* Schenk. obs. III, p. 408;” “*Lumbricus latus* Spigel. monogr.,” “Barthol. act. 1673, p. 148, t. 39;” “*Tænia vulgaris* Andry lumbr. t. 9” [but fig. 23, pl. 9, of Andry, 1718a, is clearly a *Tænia* s. str.]; “*Tænia* Bewerw. thes. 202, t. 202, f.,” “Gadd. satagund., 88.”
- 1766: *T. grysea* Pallas, 1766, 408; not accessible.
- 1781: *T. membranacea* Pallas, 1781, 59, pl. 3, figs. 13–16; not accessible.
- 1881: *T. tenella* Pallas, 1781, 69; not accessible.
- 1782: *T. lata hominis* Bloch, 1782a, 17–18.
- 1789: *T. vulgaris vel grisea vel membranacea* Fischer, 1789a, 14.
- 1789: *T. lata vel candida* Fischer, 1789a, 14.
- 1789: *T. tenella* Fischer, 1789a, 14 [T. osculis lateralibus solitariis].
- 1790: *T. vulgaris* Gmelin, 1790a, 3065–3066.
- 1802: *Tenia inermis umana* Brera, 1802a, 24–26, pl. 1, figs. 4, 5, 7, 9; in part.
- 1803: *Tænia inermis* Weber’s Brera, 1803a, 31; not Moquin-Tandon, 1860.
- 1803: *Halysis lata* (Linnæus, 1758a) Zeder, 1803a, 357–358.
- 1803: *H. membranacea* (Pallas, 1781) Zeder, 1803a, 538–539.
- 1810: *Tænia humana inermis* Rudolphi, 1810a, 71; in synonymy.
- 1816: *Botryocéphalus hominis* Lamarek, 1816, 167.

- 1819: *Bothriocephalus latus* (Linnæus, 1758a) Bremser, 1819a, 88-96, pl. 2, figs. 1-12.
 1850: *Dibothrium latum* (Linnæus, 1758a) Diesing, 1850a, 585-586.
 1873: *Bothriocephalus cristatus* Davaine, 1873a, 589-591, fig. 12.
 1876: *Tænia fenestrata* Colin, 1876a, 321.
 1880: *Bothriocephalus vulgaris cristatus* (Davaine, 1873a) Grassi, 1880a, 42.
 1880: *B. vulgaris latus* (Linnæus, 1758a) Grassi, 1880a, 42.
 1880: *B. vulgaris tenellus* (Pallas, 1781) Grassi, 1880a, 42.
 1880: *B. tenellus* (Pallas, 1781) Grassi, 1880a, 34, 42.
 1885: *Bothriocephalus latus tenellus* (Pallas, 1781) Guzzardi Asmundo, 1885a, 582.
 1886: *B. latissimus* Burgnion, 1886; not accessible.
 1886: *B. dorpatensis* Thoma in Küchenmeister, 1886c, 552.
 1886: *B. balticus* Thoma in Küchenmeister, 1886c, 552.
 1891: *Bothriocephalus latus fenestr[atus]* Maggiora, 1891, 148.
 1891: *B. fenestratus* Maggiora, 1891, 149.
 1899: *Dibothriocephalus latus* (Linnæus, 1758a) Lühe, 1899, 47.
 1899: *D. cristatus* (Davaine, 1873) Lühe, 1899, 47.

Genus ECHINOCOCCUS Rudolphi, 1801.

Species ECHINOCOCCUS GRANULOSUS (Batsch, 1786).

This species has a very complicated synonymy.

STROBILA STAGE.

- 1808: *Tænia cateniformis* of Rudolphi, 1808a, 411; misdetermined.
 1850: *T. cucumerina* Bloch of Diesing, 1850a, 532; in part only, cf. Rudolphi.
 1852: *T. serrata* [young] of Röhl, 1852, 52, figs. 1-2; misdetermined.
 1853: *T. echinococcus* Siebold, 1853, Apr. 18, 423-424, pl. 16a, figs. 1-9.
 1853: *T. serrata juvenalis röllii* Küchenmeister, 1853, 80.
 1858: *Echinococcifer* Weinland, 1858, 52; type *Tænia echinococcus*.
 1861: *Tænia nana* van Beneden, 1861a, 158-159, pl. 21, figs. 15-20.
 1861: *Echinococcifer echinococcus* (Siebold, 1853) Weinland, 1861, 19; not accessible.
 1861: *Tænia echinococca* of Kœberlé, 1861a, 329.
 1863: *T. [(Echinococcifer)] echinococcus* of Leuckart, 1863, 335-389.
 1864: *T. [(Arhynchotænia)] echinococcus* of Diesing, 1864a, 395.
 1864: *T. nana* (Beneden, 1861a) Diesing, 1864a, 395; not Siebold, 1852.
 1864: *Tænia serrata röllii* Küchenmeister of Diesing, 1864a, 395.
 1878: *T. echinoccus* Linstow, 1878, 5; misprint.
 1886: *T. [(Echinococcus)] echinococcus* of Railliet, 1886, pp. 247-252.

CYSTIC STAGE.

(a) Names based upon the granulose form, found more frequently in ruminants:

- 1782: *Tænia visceralis socialis granulosa* Goeze, 1782a, 42, 192, 258-264, pl. 20b, figs. 9-14; from sheep and calves.
 1786: *Hydatigena granulosa* Batsch, 1786a, 87-89, figs. 17, 37.
 1788: *Vesicaria granulosa* (Batsch, 1786a) Schrank, 1788, 31.
 1788: *Tænia visceralis granulosa* Goeze of Schrank, 1788, 31, and Zeder, 1800a, 305.
 1790: *T. granulosa* (Batsch, 1786a) Gmelin, 1790a, 3062-3063.
 1803: *Polycephalus granulatus* (Batsch, 1786a) Zeder, 1803a, 431-432.
 1805: *Echinococcus granulatus* (Batsch, 1786a) Rudolphi, 1805, 41, and Leuckart, 1863, 364.
 1805: *Tænia hydatigena granulosa* Rudolphi, 1805, 41; in synonymy.
 1810: *Echinococcus veterinorum* Rudolphi, 1810a, 251-253, pl. 11, figs. 5-7; *Hydatigena granulosa* Batsch, 1786a, renamed.

- 1812: *Polycephalus granosus* Lænnec, 1812, 169; *P. granulatus*, renamed.
- 1812: *Tænia granosa* Gmelin of Lænnec, 1812, 169; in synonymy.
- 1812: *T. visceralis socialis granosa* Goeze of Lænnec, 1812, 169; in synonymy.
- 1819: *Splanchnococcus echinatus* Bremser, 1819a, 249; *E. veterinorum*, renamed.
- 1850: *Tenia visceralis socialis granulosa* Goeze of Diesing, 1850a, 482; in synonymy.
- 1855: *Echinococcus scoleicipariens* Küchenmeister, 1855a, 140, pl. 3, figs. 17a-d; pl. 4, figs. 1-9, viii; *E. veterinorum*, renamed.
- 1855: *E. cænuroides* Küchenmeister, 1855a, 139; *E. veterinorum*, renamed.
- 1855: *Tænia echinococcus scoleicipariens* Küchenmeister, 1855a, x; *E. veterinorum*, renamed.
- 1866: *Echinococcus simplex* Leuckart, 1866, 779; *E. scoleicipariens*, renamed.
- 1866: *E. exogena* (Kuhn, 1830) R. Blanchard, 1886a, 433.
- 1898: *E. scolicipariens* Küchenmeister of Stiles, 1898, 113; misprint.
- (b) Names based upon the variation found more commonly in man:
- 1800: *Polycephalus hominis* Zeder, 1800a, 309-316, pl. 2, figs. 5-7.
- 1803: *P. humanus* Zeder, 1803a, 431, pl. 4, figs. 7-8; *P. hominis*, renamed.
- 1803: *P. echinococcus* Zeder, 1803a, 432; *P. hominis*, renamed.
- 1810: *Echinococcus hominis* (Zeder, 1800a) Rudolphi, 1810a, 247-250, pl. 9, fig. 4.
- 1819: *Liococcus* Bremser, 1819a, 249; *E. hominis*.
- 1819: *Splanchnococcus lævis* Bremser, 1819a, 249; *E. hominis*, renamed.
- 1855: *Echinococcus altricariens* Küchenmeister, 1855a, 133, 152-166, pl. 3, figs. 18a-19; pl. 4, figs. 10a-e; *E. hominis*, renamed.
- 1861: *Cysticercus echinococcus* (Zeder, 1803a) Kæberlé, 1861a, 183, 328, 334.
- 1863: *Echinococcus hydatidosus* Leuckart, 1863, 365; *E. altricariens*, renamed.
- 1863: *E. endogena* (Kuhn, 1830) Leuckart, 1863, 365; for *E. altricariens*.
- (c) Names based upon so-called acephalocysts:
- 1804: *Acephalocystis* Lænnec, 1804, 132, 134-135 (no specific names mentioned); 1812, 96-123, 130-155, 170-173.
- 1808: *A. humana* Lüdersen; not accessible; see Tschudi, 1837, 35.
- 1808: *A. suilla* Lüdersen; not accessible; see Tschudi, 1837, 36.
- 1812: *A. ovoidea* Lænnec, 1812, 171.
- 1812: *A. cystifera* Lænnec, 1812, 171.
- 1812: *A. ansa* Lænnec, 1812, 172.
- 1812: *A. intersecta* Lænnec, 1812, 172.
- 1812: *A. surculigera* Lænnec, 1812, 172.
- 1812: *A. granosa* Lænnec, 1812, 172.
- [1812: *A. plana* Lænnec, 1812, 172-173, is a spurious parasite, albuminous concretions occasionally found in the wrist; afterwards described by Dupuytren as *Ovuligera carpi*.]
- 1821: *Acephalocystus communis* Merat, 1821, 229.
- 1825: *Acephalocystis communis* Lænnec, 1825, 32.
- 1829: *A. eremita* Cruveilhier, 1829a, 198; the most frequent in animals.
- 1829: *A. sterilis* Cruveilhier, 1829a, 198; same as *A. eremita*.
- 1829: *A. socialis* Cruveilhier, 1829a, 198.
- 1829: *A. prolifera* Cruveilhier, 1829a, 198; same as *A. socialis*.
- 1829: *Acephalocystis socialis* Cruveilhier, 1829a, 198.
- 1829: *A. prolifera* Cruveilhier, 1829a, 198.
- 1830: *Acephalocystis endogena* Kuhn, 1830, not accessible; 1832, 890, in man; *A. socialis vel prolifera*, renamed.
- 1830: *A. exogena* Kuhn, 1830, not accessible; 1832, 890; in animals; *A. eremita vel sterilis*, renamed.
- 1833: *A. granulosa* delle Chiaje, 1833a, 32; for *A. granosa* Lænnec, 1804.
- 1833: *A. eremita sterilis* Cruveilhier of delle Chiaje, 1833a, 33.
- 1833: *A. prolifera socialis* Cruveilhier of delle Chiaje, 1833a, 33.

1844: *A. simplex* Goodsir, 1844d, 282.

1861: "*Acephalocystis macaci?*" Cobbold, 1861e, 120.

1861: ?*A. ovis tragelaphi* Cobbold, 1861e, 120; "probably an aborted coenurus."

(d) Names based upon names of animals in which the parasite occurs:

1800: *Polycephalus hominis* Zeder, 1800a, 309–316, pl. 2, figs. 5–7.

1803: *P. humanus* Zeder, 1803a, 431; *P. hominis*, renamed.

1808: *Acephalocystis humana* Lüdersen, 1808; not accessible.

1808: *A. suilla* Lüdersen, 1808; not accessible.

1810: *Echinococcus hominis* (Zeder, 1800a) Rudolphi, 1810a, 247–250.

1810: *E. simiæ* Rudolphi, 1810a, 250–251; *Hydatis erratica* Blumenbach, 1805, renamed.

1815: *E. simiæ cynomolgi* Oken, 1815, 142.

1847: *E. giraffæ* Gervais, 1847a, 100–102.

1850: *E. giraffæ* Gervais of Diesing, 1850a, 483.

—?: *E. suis*; not traced.

1848: *E. arietis* E. Blanchard, 1848; not accessible at present.

1852: *E. pardi* Huxley; not traced.

1861: "*Acephalocystis macaci?*" Cobbold, 1861e, 120.

1861: ?*A. ovis tragelaphi* Cobbold, 1861e, 120; "probably an aborted coenurus."

(e) Names based upon names of organs in which the parasite occurs:

1862: *Echinococcus cerebri* Spiering, 1862, 13; not accessible.

1862: *E. hepatis* Scholler, 1862, 14, not accessible; Kehlberg, 1873.

1862: *E. process. vermiformis* Scholler, 1862, 14; not accessible.

1867: *E. lienis* Ber. Krankenanst. Rudolf-Stiftung, Wien, 1867, 237; Kehlberg, 1873a.

1875: *E. pulmonum* Huppert, 1875a.

1880: *E. intracranialis* Fricke, 1880a, 5.

1886: *E. retroperitonealis* Bitter, 1886a.

1891: *E. mesenterii* Surmann, 1891.

1895: *E. subdiaphragmalis-præperitonealis* Krasnoff, 1895a, 852–863.

1896: *E. subphrenicus* Huber, 1896a, 527.

1898: *E. intercranialis* Fricke of Stiles, 1898, 113; misprint.

1898: *E. retroperitonealis* Bitter, 1886, of Stiles, 1898, 113; misprint.

—?: "*E. cerebralis* Perroncito," not accessible; possibly based upon "*Echinococchi cerebrali*" Perroncito, 1882, 172.

(f) General names, proposed to include several or all variations:

1827: *Echinococcus infusorium* F. S. Leuckart, 1827, 15.

1837: *Polycephalus volvox* Tschudi, 1837, 31.

1837: *P. echinococcus* Tschudi, 1837, 26–27, 38–45.

1837: ?*E. variabilis* Siebold, 1837, 184, not accessible; see *E. variabilis* Huxley, 1852.

1850: *E. polymorphus* Diesing, 1850a, 482–484.

1891: *E. cysticus* Huber, 1891b; *E. polymorphus*, renamed.

1896: *E. unilocularis*, see Huber, 1896a, 506, as syn. of *E. cysticus*.

(g) Other names:

1776: *Hydatides singulares* Pallas, 1766, 172–174; in animals and man; doubtful whether this should be recognized in a nomenclatural sense.

1805: *Hydatis erratica* Blumenbach, 1805a, 2 pp., 5 figs.; 1816a, 13; renamed *E. simiæ* Rudolphi, 1810a.

1810: *Finna idatoides* Brera, 1810a, 164–168, pl. 3, figs. 1–3, in man.

1825: "*Hydatis simplex* Home" of delle Chiaje, 1833a, 33; *Acephalocystis eremita sterilis*.

1844: ?*Astoma acephalocystis* Goodsir, 1844d, 282; supposed to be an hydatid.

1844: ?*Diskostoma acephalocystis* Goodsir in Gairdner, 1844a, 276; Goodsir, 1844d, 282; supposed to be an hydatid.

1852: *Echinococcus variabilis* Huxley, 1852a, 123; 1898a, 211, 213.

1875: *E. unilocularis* Haffter, 1875a, 365.

1882: *E. multiplex* Stiller, 1882, 352; in man.

Subspecies **ECHINOCOCCUS GRANULOSUS MULTILOCULARIS** (Leuckart, 1863).

- 1856: Die multiloculäre, ulcerirende Echinokokkengeschwulst Virchow, 1856, 84–95.
 1863: *Echinococcus multilocularis* Leuckart, 1863, 360, 369, 370, fig. 110; Blanchard, 1886a, 447.
 1868: Tumeur hydatique alvéolaire Carrière, 1868a; 1869a.
 1875: *Echinococcus multilocularis hepatis* Haffter, 1875a, 362–371.
 1883: *E. alveolaris* Klemm, 1883, not accessible; Blanchard, 1886a, 447.
 1886: ? *E. racemosus* Leuckart, 1886, 795, fig. 334.
 1896: *E. multilocularis exulcerans* Huber, 1896a, 506.
 1896: *E. osteoklastes* Huber, 1896a, 506.
 1905: *Tænia echinococcus alveolaris* (Klemm, 1883) Devé, 1905, Jan. 27, 128.

There is some difference of opinion in regard to the status of the multilocular echinococcus, some authors regarding it as specifically identical with the type form, others regarding it as distinct. From the views advanced, and because of its geographic distribution, it seems to me that this form may be given subspecific rank at least, and that it will probably be eventually recognized as of specific rank.

REJECTION OF NAMES.

Art. 32. A generic or a specific name, once published, can not be rejected, even by its author, because of inappropriateness. Examples: Names like *Polyodon*, *Apus*, *albus*, etc., when once published, are not to be rejected because of a claim that they indicate characters contradictory to those possessed by the animals in question.

DISCUSSION.—It is not infrequent that authors reject a name because they consider it nondescriptive or inappropriate, but the code does not recognize this as sufficient reason for such action. In this connection it is essential to recall that names are not definitions; they are simply handles by which objects are known. When an animal is known as *albus*, this name does not necessarily mean that the animal is white, but the combination of the letters *a-l-b-u-s* is simply a designation by which this animal is known.

This view appears very illogical, at first sight, to nonzoologists, but it is not so illogical as it may seem. On the contrary, it corresponds to everyday experience. If a man has the name Black, Green, or Brown, we do not change it on the ground that he is white, nor do we change the name of a negro named White simply because his skin is black. The nomenclaturalist sees no more reason for changing names of animals because they are not descriptive than other people do in case of family names of persons.

In a name we do not look for a summary of the characters of an animal; that summary we expect to find in the description, known technically as the “diagnosis.”

The fact that “*Amæba coli*” was reported for other parts of the body than the colon has no bearing on the nomenclature of the species;

hence a change of name to "*Amœba dysenterix*," on basis of pathological findings, was not in accord with the code.

Were we to admit "appropriateness" as a prerequisite to a name and were we to take a vote to determine which of the 110 names of the parasite of hydatid disease is the most appropriate, it would be difficult to reach an agreement. Under the code, however, the subjective element of "appropriateness" is entirely eliminated.

Another point which some persons find difficulty in understanding is the fact that we do not concede to the author of a name any rights over that name which are not common to all zoologists. We recognize no name in nomenclature until it is published; when once published it is common property; if it has been published with lack of due consideration, its author is still responsible for its publication; after it is once published it becomes subject to the code, and were the code to give to the original author any rights over the name which other authors did not possess there would be little or no outlook for stability of that name until after its author's death; in the meantime the name may have come into general use, and if just before its author's death he decided to change it because a "more appropriate" name occurred to him or because of some other subjective reason, the nomenclature of the group in question might have to undergo a complete and unnecessary change.

In understanding this and all other points of nomenclature it is essential to recall that the question of "giving a man credit" for his work is of very secondary consideration. The entire code, while not ignoring justice, is based primarily upon practical rather than upon sentimental considerations, and is intended to prevent an inconvenience being caused to the entire scientific world rather than to protect an individual who works without a due regard of his responsibilities to future generations.

Art. 33. A name is not to be rejected because of tautonymy, that is, because the specific or the specific and subspecific names are identical with the generic name. Examples: *Trutta trutta*, *Apus apus apus*.

DISCUSSION.—Some authors object to tautonymy, as *Trutta trutta*, *Heterophyes heterophyes*, on the ground that they do not consider such combinations euphonic. Nomenclature, however, is neither poetry nor music. It is a practical, not a sentimental, proposition. By application of the law of priority tautonymy is sometimes inevitable, and as the law of priority is the keystone of nomenclature, tautonymy is accepted.

Personally I not only do not object to tautonymy, but I am strongly in favor of it. When we refer to *Tænia solium* it is a question of memory or of looking up references which recalls to our mind that *solium* is the type of *Tænia*. When we refer to *Heterophyes heterophyes*, however, the name itself shows us that we are dealing with the type of the genus.

Art. 34. A generic name is to be rejected as a homonym when it has previously been used for some other genus^a of animals. Example: *Trichina* Owen, 1835, nematode, is rejected as homonym of *Trichina* Meigen, 1830, insect.

DISCUSSION.—This plan of rejecting a name on the ground that it has been used for some other genus has met with opposition from several sources, but though it may at first appear Draconian, it seems necessary. If identical generic names were accepted in different groups, on the ground that a protozoon would not be likely to be confused with a worm or an insect, we might be brought to a very involved position. Imagine, for instance, the lucidity of an article on the relation of zoology to medicine in which were discussed *Distoma a* as a protozoon, *Distoma b* as a medicinal sponge, *Distoma c* as a trematode, *Distoma d* as a tapeworm, *Distoma e* as a nematode, *Distoma f* as a thorn-headed worm, *Distoma g* as a mite, *Distoma h* as a mosquito, and *Distoma i* as a poisonous snake. Any code of nomenclature which would make such a condition theoretically possible would bring about the very confusion which nomenclature seeks to avoid.

Protest has been raised against rejecting *Trichina*, 1835, as generic name of *Trichina spiralis*; that this rejection is unfortunate may be readily admitted, but with an earlier insect genus named *Trichina*, 1830, zoologists can hardly be expected to admit *Trichina* as valid name for a nematode genus.

Mallory proposed *Cyclaster*, 1904, as generic name for the organism which he found in a case of scarlet fever, but as this same name was

^a Besides the special journals and special nomenclators of various groups, authors will find the following publications very valuable in determining whether any given generic or supergeneric name is preoccupied, and if authors will consult these works before publishing new names, considerable confusion and later change of names will be avoided:

C. D. Sherborn, *Index animalium sive index nominum quæ ab A. D. 1758, generibus et speciebus animalium imposita sunt. Societatibus eruditorum adiuvantibus a Carolo Davis Sherborn confectus. Sectio I a kalendis januariis, 1758, usque ad finem decembris, 1800.* Cantabrigiæ, 1902, 8°.

S. H. Scudder, *Nomenclator zoologicus. An alphabetical list of all generic names that have been employed by naturalists for recent and fossil animals from the earliest times to the close of the year 1879.* In 2 parts: I. Supplemental list. II. Universal index. Washington, 1882, 8°.

C. O. Waterhouse, *Index zoologicus. An alphabetical list of names of genera and subgenera proposed for use in zoology as recorded in the Zoological Record, 1880–1900, together with other names not included in the Nomenclator zoologicus of S. H. Scudder.* Compiled . . . by Charles Owen Waterhouse and edited by David Sharp. London, 1902, 8°.

The Zoological Record, XXXVIII [et sequ.]. *Being records of zoological literature relating chiefly to the year 1901* [et sequ.]. London, 1902 [et sequ.], 8°. Index to names of new genera and subgenera.

Register zum zoologischen Anzeiger. Herausgegeben von J. V. Carus, Jahrgang 1–10 (1878–1887), 11–15 (1888–1892), 16–20 (1893–1897), 21–25 (1898–1902). Leipzig, 1889, 1893, 1899, 1903, 8°.

used in 1856 for a genus of echinoderms, Mallory was entirely justified in recently changing the name of his genus to *Cyclasterion*, 1905.

Art. 35. A specific name is to be rejected as a homonym when it has previously been used from some other species of the same genus. Example: *Tænia ovilla* Rivolta, 1878 (n. sp.) is rejected as homonym of *T. ovilla* Gmelin, 1790.

When in consequence of the union of two genera, two different animals having the same specific or subspecific name are brought into one genus, the more recent specific or subspecific name is to be rejected as a homonym.

DISCUSSION.—This rule scarcely needs any justification. To retain the same specific name for two or more different species in one genus would be to invite hopeless confusion.

As a general proposition it is well to avoid the introduction of a new specific name into a genus if the same name is used in another genus of the same family.

Art. 36. Rejected homonyms^a can never be again used. Rejected synonyms can again be used in case of the restoration of erroneously suppressed groups. Example: *Tænia Giardi* Moniez, 1879, was suppressed as a synonym of *Tænia ovilla* Rivolta, 1878; later it was discovered that *Tænia ovilla* was preoccupied (*Tænia ovilla* Gmelin, 1790). *Tænia ovilla*, 1878, is suppressed as a homonym, and can never again be used; it was stillborn and can not be brought to life, even when the species is placed in another genus (*Thysanosoma*). *Tænia Giardi*, 1879, which was suppressed as a synonym, becomes valid upon the suppression of the homonym *Tænia ovilla* Rivolta.

DISCUSSION.—This rule is opposed by some authors, but it is in the interest of uniformity. It insures the use of the same specific name for a given species by authors who recognize the use of subgenera, as is used by authors who do not recognize subgenera.

RECOMMENDATIONS.—It is well to avoid the introduction of new generic names which differ from generic names already in use only in termination or in a slight variation in spelling which might lead to confusion. But when once introduced such names are not to be rejected on this account. Examples: *Picus*, *Pica*; *Polyodus*, *Polyodon*, *Polyodonta*, *Polyodontas*, *Polyodontus*; *Macrodon*, *Microdon*.

The same recommendation applies to new specific names in any given genus. Examples: *necator*, *necatrix*; *furcigera*, *furcifera*; *rhopalocephala*, *rhopaliocephala*.

If from the radical of a geographic name two or more adjectives are derived, it is not advisable to use more than one of them as specific name in the same genus, but if once introduced, they are not to be rejected on this account. Examples: *hispanus*, *hispanicus*; *moluccensis*, *moluccanus*; *sinensis*, *sinicus*, *chinensis*; *cylonicus*, *zeylanicus*.

The same recommendation applies also to other words derived from the same radical and differing from each other only in termination or by a simple change in spelling. Examples: *cæruleus*, *cæruleus*; *silvestris*, *sylvestris*, *silvaticus*, *sylvaticus*; *littoralis*, *litoralis*; *autumnalis*, *auctumnalis*; *dama*, *damma*; *fluvialis*, *fluviatilis*, *fluviaticus*.

^a A homonym is one and the same name for two or more different things. Synonyms are different names for one and the same thing.

APPENDIX.

A. It is very desirable that the proposition of every new systematic group should be accompanied by a diagnosis, both individual and differential, of said group in English, French, German, Italian, or Latin. This diagnosis should state in what museum the type specimen has been deposited and should give the museum number of said specimen.

B. In publications issued in any other language than English, French, German, Italian, or Latin it is very desirable that the explanation of figures be translated into one of these tongues.

C. The metric system of weights and measures and the centigrade thermometer of Celsius are adopted as standard. The *micron* (0.001mm.), represented by the Greek letter μ , is adopted as the unit of measure in microscopic work.

D. The indication of enlargement or of reduction, which is very desirable for the comprehension of an illustration, should be expressed in figures rather than by mentioning the system of lenses used.

E. The indication of enlargement or reduction of an object is usually linear. The sign of multiplication is used for enlargement, and the fraction for reduction. Examples: $\times 50$ indicates that the object is enlarged 50 times; $\frac{1}{50}$ indicates that it is reduced to $\frac{1}{50}$ th.

If it is desired to specify that the enlargement is linear, surface, or mass, this may be done as follows: $\times 50^1$ indicates linear enlargement; $\times 50^2$ indicates surface enlargement; $\times 50^3$ indicates mass enlargement.

F. Transcription of Greek words:

The following table indicates the manner in which Greek words should be transcribed:

$\varepsilon = e$	(ὕαλος)	— Hyalea, <i>not</i> Hyalæa.
$\eta = e$	(πειρήνη)	— Pirena, <i>not</i> Pirina.
final $\eta = a$	(πειρήνη)	— Pirena, <i>not</i> Pirene.
$\theta = th$	(τηθύς)	— Tethys, <i>not</i> Tetys.
$\iota = i$	(βαλίας)	— Balia, <i>not</i> Balea.
$\kappa = c$	(ἵπποκρήνη)	— Hippocrena, <i>not</i> Hippochrenes.
$\xi = x$	(ξένος)	— Xenus, Xenophora.
$\rho = r$	(πτέρων)	— Pterum.
$\upsilon = y$	(ὕβος)	— Hybolithus, <i>not</i> Hibolites.
$\alpha\iota = ae$	(λιμναῖος)	— Limnæa, <i>not</i> Limnea.
$\alpha\upsilon = au$	(γλαυκός)	— Glaucus.
$\epsilon\iota = i$	(χεῖλος)	— Chilostomum, <i>not</i> Cheilostoma.
$\epsilon\upsilon = eu$	(εὕρος)	— Eurus.

$\omega, \omicron = oe$ ($\omicron\acute{\iota}\acute{\kappa}\acute{\epsilon}\omega$)	— Dioeca, Dendrœca, <i>not</i> Dioica, Dendroica.
final $ov = um$ ($\acute{\epsilon}\phi\acute{\iota}\pi\pi\acute{\iota}\omicron\nu$)	— Ephippium, <i>not</i> Ephippion.
final $os = us$ ($\acute{\omicron}\mu\phi\alpha\lambda\acute{\omicron}\varsigma$)	— Euomphalus, <i>not</i> Euomphalos.
$ou = u$ ($\lambda\omicron\upsilon\tau\acute{\eta}\rho\acute{\iota}\omicron\nu$)	— Luterium, <i>not</i> Lotorium.
$\gamma\gamma = ng$ ($\acute{\alpha}\gamma\gamma\alpha\rho\acute{\epsilon}\acute{\iota}\alpha$)	— Angaria.
$\gamma\chi = nch$ ($\acute{\alpha}\gamma\chi\acute{\iota}\sigma\tau\omicron\mu\omicron\nu$)	— Anchistomum, <i>not</i> Angistoma.
$\gamma\kappa = nc$ ($\acute{\alpha}\nu\kappa\acute{\iota}\sigma\tau\rho\omicron\nu$)	— Ancistrodon, <i>not</i> Agkistrodon.
$\rho = rh$ ($\rho\acute{\epsilon}\acute{\alpha}$)	— Rhea.
$\acute{\epsilon} = he$ ($\acute{\epsilon}\rho\mu\alpha\acute{\iota}\alpha$)	— Hermæa, <i>not</i> Ermæa.

G. Transcription of geographic and proper names.

The geographic names of nations which employ the Latin characters are to be written with the orthography of the country in which they originate.

The following rules apply only to the geographic names of countries which have no true alphabet or which use letters that are different from the Latin alphabet.

Names of places, however, which have been established by long usage preserve their usual orthography. Examples: *Algiers, Moscow*.

1. The vowels *a, e, i,* and *o* are pronounced as in French, Italian, Spanish, or German. The letter *e* is never mute.

2. The French sound *u* is represented by *ü* with dieresis, as in German.

3. The French sound *ou* is represented by *u*, as in Italian, Spanish, German, etc.

4. The French sound *eu* is represented by *æ*, pronounced as in the French word *œil*.

5. The long sound of a vowel is indicated by a circumflex accent; the interrupted sound is indicated by an apostrophe.

6. The consonants *b, d, f, j, k, l, m, n, p, q, r, t, v,* and *z* are pronounced as in French.

7. The letters *g* and *s* always have the hard sound, as in the French words *gamelle* and *sirop*.

8. The sound represented in French by *ch* is designated by *sh*. Examples: *sherif, Kashgar*.

9. *Kh* represents the harsh guttural; *gh* represents the soft guttural of the Arabs.

10. *Th* represents the sound which terminates the English word *path* (*θ* in Greek). *Dh* represents the sound which commences the English word *those*.

11. Aside from such employment (9, 10) of the letter *h* modifying the letter which precedes it, *h* is always aspirated; the apostrophe is therefore never used before a word commencing with *h*.

12. The semivowel represented by *y* is pronounced as in *yole*.

13. The semivowel *w* is pronounced as in the English word *William*.

14. The double sounds *dj*, *tch*, *ts*, etc., are indicated by letters representing the sounds which compose them. Example: *Matshim*.

15. The *ñ* is pronounced *gn*, as in *seigneur*.

16. The letters *x*, *c*, and *q* are not used, since they are duplicates of other letters representing the same sounds; but *q* may serve to indicate the Arabic *qaf* and the soft aspirate may be used to represent the Arabic *aïn*.

An attempt should be made to indicate as exactly as possible, by means of the letters given above, the local pronunciation without trying to give a complete representation of all the sounds which are heard.



TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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M. J. ROSENAU, Director.

June, 1906

ILLUSTRATED KEY

TO THE

CESTODE PARASITES OF MAN.

BY

CH. WARDELL STILES.



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3906.

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ILLUSTRATED KEY TO THE CESTODE PARASITES OF MAN.

By CH. WARDELL STILES, PH. D., Chief of Division of Zoology, Hygienic Laboratory,
U. S. Public Health and Marine-Hospital Service.

INTRODUCTION.

The present paper is intended as a companion to the "Illustrated Key to the Trematode Parasites of Man," Bull. 17, of this laboratory, and includes all of the cestodes, both adults (tapeworms) and larvæ (bladder worms) known to occur in man.

The more important species for American physicians are at present: *Tænia saginata*, *T. solium*, *Hymenolepis nana*, *Echinococcus*, and *Dibothriocephalus latus*. In addition to these, *Tænia confusa* may prove to be an important parasite, more particularly in the Northwest. It is a little difficult to forecast which forms will prove to be of importance in the Philippines, but in addition to the first five species mentioned above, *Diplogonoporus grandis* and *Sparganum mansoni* should be held in mind as possibilities.

CLINICAL CLASSIFICATION OF CESTODE INFECTIONS (TÆNIASES).

Tænia was the original (1758) genus of tapeworms, and infections by any member of the group may conveniently be referred to as tæniasis. The following clinical forms may be distinguished:

Intestinal tæniasis: This is the more common form and includes the infection with adult tapeworms; diagnosis by finding the segments in the stools, in the bed, or in the clothes, or by finding the eggs in microscopic examination of the stools; treatment medicinal, by administering tæniacides or tæniafuges (male fern, cusso, kamala, pomegranate, pumpkin seed, etc.) (p. 11).

Somatic tæniasis: This includes infections of muscles, connective tissue, liver, lungs, brain, eye, or other organs, with the larval stage of tapeworms, and we may distinguish—

- (a) *Cysticercosis*: Infection with the larva of *Tænia solium*, known as *Cysticercus cellulosæ*, which occurs chiefly in the muscles, connective tissue, eye, and brain; diagnosis by excision, or by ophthalmoscopic examination, or by symptoms, especially when combined with a history of intestinal infection with *Tænia solium*; treatment surgical (p. 68).

- (b) *Echinococcosis*: Infection with the hydatid stage of *Echinococcus* of dogs; it may occur in any organ, but chiefly in liver and lungs; diagnosis by symptoms or by aspiration and microscopic examination of the fluid to find the hooks or the heads; treatment surgical (p. 75).
- (c) Infection with *Sparganum mansoni*; rare; diagnosis by finding the worm; treatment surgical, or by extraction of worm per urethram (p. 83).
- (d) Infection with *Sparganum proliferum*; rare; Japan; diagnosis by finding the worm; treatment surgical (p. 86).

THE PARASITES OF TÆNIASIS.

The cestodes differ from the trematodes by the usual presence of a distinct head with 2 or 4 suckers, by the segmented condition of the adult, each segment or proglottid representing, roughly speaking, a single trematode, so that the entire chain (strobila) may be viewed as a colony, and by the absence of an intestine. All of the species found in man are hermaphrodites.

ANATOMICAL STRUCTURE OF CESTODES.

The following technical description shows the systematic position and anatomical structure of the tapeworms under discussion:

Superfamily *Dibothriocephaloidea*.

Family *Dibothriocephalidæ*.

Genera *Dibothriocephalus*, *Diplogonoporus*, and *Sparganum*.

Superfamily *Tænioidea*.

Family *Tæniidæ*.

Subfamily *Dipylidiinæ*.

Genera *Dipylidium* and *Hymenolepis*.

Subfamily *Davaineinæ*.

Genus *Davainea*.

Subfamily *Tæniinæ*.

Genera *Tænia* (with subgenera *Tænia* and *Tæniarhynchus*) and *Echinococcus*.

The head or scolex is provided with 2 (*Dibothriocephalidæ*) or 4 (*Tæniidæ*) suckers (*acetabula*) which may (*Davainea*) be provided with hooks; on its apex it has (*Tæniidæ*) a *rostellum*, which in most species is armed with hooks; the head contains the brain and in some worms a circular excretory ring. *Lateral nerves* extend from the brain through the entire strobila to the distal end. *Lateral canals* extend from the circular ring distally through the segments; in the *Tæniidæ* are distinguished *dorsal* and *ventral canals*, the latter being connected at the distal end of each segment by a *transverse canal*. The head is followed by a *neck*, which segments transversely to form the *proglottides*. Each proglottid or segment contains a full set (in some cases two sets) of both male and female organs. The *genital pores* are lateral (*Tæniidæ*) or ventral (*Dibothriocephalidæ*). The *male glands* consist of *testicles*, which vary in number; from these extend *vasa efferentia* which collect to form the *vas deferens*; the latter enters the *cirrus-pouch*, from which the *cirrus* (penis) is extruded. The *female* opening is close to the cirrus; the *vagina* runs toward the genital glands, swelling to a *receptaculum seminis*; the glands are: *shell gland*, *ovary*, and *vitellogene gland*; the

fertilized egg enters the *uterus*. These different organs vary in different genera and species (see keys, pp. 11, 15, 25, 48, 51, 62).

The embryo (*onchosphere*) is provided with 6 minute hooks; it enters an intermediate host and develops into a so-called larval stage (cysticercus, echinococcus, cysticercoid, plerocercoid), in which the head forms; upon being swallowed by the final host, the head attaches itself to the intestine and the segments form by transverse strobilation of the neck.

INTESTINAL TÆNIASIS.

From a clinical point of view the most important tapeworms for man are at present three large forms (*Tænia saginata*, *T. solium*, and *Dibothriocephalus latus*) and one small species (*Hymenolepis nana*); in fact, nearly our entire knowledge of intestinal tæniasis in man is based upon these four species. The other species reported for man are relatively of less importance, since they are less frequent. The following genera are reported for man:

KEY^a TO GENERA OF ADULT CESTODES FOUND IN MAN.

(For genera thus far reported for man in the United States, follow roman type.)

1. Head with two elongate or slit-like suckers; uterus forms a rosette; genital pores ventral 2
- Head with four cup-shaped suckers; uterus does not form a rosette; genital pores lateral (marginal) 3

DIBOTHRIOCEPHALIDÆ.

2. Single set of genital pores and uteri present in ventro-median line; chiefly Old World *Dibothriocephalus* (p. 15)
- Double set of pores and uteri present in ventro-submedian lines; Asiatic *Diplogonoporus* (p. 21)

TÆNIIDÆ.

3. Large forms; gravid segments over one-third of an inch (9 to 35 mm.) long; uterus median with lateral branches *Tænia* (p. 24)
- Smaller forms; ripe segments less than one-third of an inch (to 7 mm.) long 4
4. Genital pores single; rostellum with not more than 2 rows of hooks 5
- Genital pores double; rostellum with several rows of hooks *Dipylidium* (p. 48)
5. Suckers not armed; 3 testicles in each segment *Hymenolepis* (p. 51)
- Suckers armed with hooks; about 15 to 50 testicles in each segment *Davainea* (p. 62)

CLINICAL DIAGNOSIS OF INTESTINAL TÆNIASIS.

The clinical diagnosis of intestinal tapeworms may be made by finding the segments passed from the anus, or by microscopic examination of the stools to find the eggs. For the microscopic examination no special technique is required. Take a small amount of fecal matter on the end of a match or toothpick (using a separate one for each stool), smear this in a drop of water on a slide, cover with cover slip,

^aThis key is based primarily upon the species found in man, and on this account should not be relied upon for other species found in other animals.

and examine first under a medium-power and later under a high-power dry lens. In some cases (*Dibothriocephalus* and *Diplogonoporus*) there is a chance of confusing the eggs with those of trematodes: see key, p. 9, in Illustrated Key to Trematode Parasites of Man. In these examinations the 2 by 3 slide is more convenient to work with than the ordinary 1 by 3 slide.

KEY TO THE EGGS OF TAPEWORMS REPORTED FOR MAN.

(For species thus far found in man in the United States follow roman type.)

1. Eggs provided with a "cap" or operculum, like the egg of certain liver flukes, but not containing an embryo when found in the stools: *Dibothriocephalidæ* 9
- Eggs not provided with "cap" or operculum: round to oval; may occur in clusters ("egg sacks"), and always contain a 6-hooked embryo (onchosphere) when found in the stools: *Tæniidæ* 2

TÆNIIDÆ.

2. Egg with thick, radially striated inner shell (embryophore): *Tæniinæ* 3
- Egg with thin, membranous, inner shell 6

TÆNIA.^a

3. Occurrence in man doubtful; rare if they occur at all 5
- Positively known to occur in man 4
4. Embryophore (inner shell) ovoid, rusty brown, 35 to 40 by 20 to 30 μ : outer shell delicate with 1 or 2 polar filaments, not usually present on eggs in feces: this is the most common *Tænia* in the United States: the fat tapeworm *Tænia saginata* (p. 27)
- Embryophore almost round, usually brown, 31 to 36 μ ; comparatively rare in the United States; the pork tapeworm *T. solium* (p. 37)
- Embryophore oval, whitish to yellowish, 39 by 30 μ ; reported for Nebraska; Ward's tapeworm *T. confusa* (p. 44)
- Embryophore 31 to 39 by 33.8 μ ; reported for Africa *T. africana* (p. 32)
- Egg unknown; reported for Asiatic Russia *T. hominis* (p. 36)
5. Embryophore ovoid, 36 to 40 by 31 to 36 μ *T. pisiformis* (p. 41)
- Embryophore globular, 31 to 37 μ *T. teniaformis* (p. 43)
6. Eggs occur in egg-sacks 8
- Eggs do not occur in egg-sacks 7

HYMENOLEPIS.

7. Eggs oval or globular; 2 distinct membranes; outer membrane 30 to 60 μ ; inner membrane 16 to 34 μ , presenting at each pole a more or less conspicuous mammillate projection: common in some localities; the dwarf tapeworm *H. nana* (p. 51)
- Eggs round or slightly oval; outer membrane 54 to 86 μ ; yellowish, may be radially striated; inner membrane 24 to 40 by 20 to 35 μ , with mammillate projection at each pole, often not apparent: rare in man *H. diminuta* (p. 54)
- Eggs oval or spherical; outer membrane 50 to 100 by 35 to 100 μ ; inner membrane 30 to 40 by 25 μ , occasionally with polar papillæ; exceedingly rare in man *H. lanceolata* (p. 58)

^a It is not always safe to rely upon the egg alone in distinguishing the different species.

DIPYLIDIUM AND DAVAINEA.

8. Eggs spherical, 43 to 50 μ ; 8 to 20 eggs in each egg capsule; accidental in man, chiefly in children.....*Dipylidium caninum* (p. 50)
 Eggs with 2 shells, the outer with 2 mammillate projections; onchosphere (embryo) 8 μ ; 1 to 3 eggs in each egg-ball, with calcareous corpuscles; tropical and subtropical*Davainea madagascariensis* (p. 63)
 Mature eggs not yet observed, but probably about 38.6 by 36.4 μ ; egg-balls without calcareous corpuscles; Asiatic*D. asiatica* (p. 65)

DIBOTHRIOCEPHALIDÆ.

9. Eggs 68 to 71 by 45 to 50 μ ; chiefly Old-World form, occasionally in America; the broad tapeworm*Dibothriocephalus latus* (p. 15)
 Eggs 75 to 80 by 50 μ ; Greenland*D. cordatus* (p. 19)
 Eggs brownish, 63 by 48 to 50 μ ; Asiatic*Diplogonoporus grandis* (p. 22)

SYMPTOMS.

The symptomatology of intestinal tæniasis is indefinite. There may be giddiness, humming in the ears, disorders of vision, nasal and anal pruritus, salivation, disorders of appetite and digestion, colic, pains in epigastrium and other regions of abdomen, cardiac palpitation, syncope, pains and lassitude in limbs, emaciation, anemia, etc.

TREATMENT.

In treatment it should be recalled that (a) the clearer the bowels are the better are the chances for success, (b) the older the drug is the less are the chances for success, and (c) the nervous system of the tapeworm is well developed, hence the parasites are susceptible to a sudden change in temperature.

(a) *Preparation of patient*.—Clear out the bowels, so that the drug can reach the parasite and so that the latter will not meet with obstructions while descending to the anus. The diet should be light, avoiding vegetables and any foods which tend to the production of large quantities of feces.

(b) *Anthelmintic*.—Doubtless many failures in treatment are due to using old drugs which have lost their anthelmintic properties.

(c) *Passage of the worm*.—The patient should be instructed to pass the worm into a vessel containing warm water. Under no circumstances should he pass the worm into a water-closet, as the parasite, upon coming in contact with a cold object, may contract and break.

PREVENTION.—The method of prevention varies according to the different species. As all intestinal tapeworms are contracted *per os*, prevention involves a care of the food eaten. All tapeworm segments and stools should be burned, unless used for scientific study. See also under the different species.

Superfamily DIBOTHRIOCEPHALOIDEA.^a

ORDINAL DIAGNOSIS.—*Cestoda*: Scolex armed or unarmed, with two groove-like suckers, situated dorsally and ventrally; they are usually not highly developed, but in some cases are considerably modified by development of their walls, or by more or less coalescence of their margins; or they may unite to form a single apical sucker, or may become rudimentary, their function being performed by an unpaired apical sucker; in some cases a pseudoscolex may form. Neck present or absent. External segmentation present or absent. Three genital pores present; uterine pore is always on one of the surfaces; the vaginal and cirrus pores may be on the same surface as the uterine or on the opposite surface or marginal. Genital organs usually single, rarely double. Their development progresses from anterior end posteriorly, but does not pass the mature stage into an atrophying stage. Testicles numerous, situated in two more or less separated lateral fields in the medullary layer; vas deferens always highly developed, usually forming a coil. Ovary distinctly or indistinctly bipartite, situated in distal portion of segment, usually median in forms with single series of genitalia; in forms with double series, submedian; in forms with lateral pores, on side of median line toward the pore. "Schluckorgan" always present. Vitellogene glands with numerous follicles, situated in two, more or less separated lateral fields, nearly always dorsal and ventral, and usually in cortical layers. Eggs quite similar to those of *Fasciola*, but not always with operculum.

TYPE FAMILY.—*Dibothriocephalidæ*.

This superfamily may be divided into two families (*Dibothriocephalidæ* and *Ptychobothriidæ*), only one of which furnishes parasites to man, namely:

Family DIBOTHRIOCEPHALIDÆ^b Luehe, 1899, emend. Braun, 1903.

FAMILY DIAGNOSIS.—*Dibothriocephaloidea* (p. 14): Uterus forms a rosette. Eggs with operculum.

TYPE GENUS.—*Dibothriocephalus* Luehe, 1899.

This family is divided into 4 subfamilies (*Tricuspidariinæ*, *Dibothriocephalinæ*, *Ligulinæ*, and *Cyathocephalinæ*), only one of which is represented among the intestinal parasites of man, namely:

Subfamily DIBOTHRIOCEPHALINÆ Luehe, 1899.

SUBFAMILY DIAGNOSIS.—*Dibothriocephalidæ* (p. 14): Scolex unarmed; suckers either two small grooves (one dorsal and one ventral) or two funnel-shaped organs with highly developed borders, or by coalescence of their borders changed to sucker-tubes, or rudimentary and then replaced by an apical sucker. Neck present or absent. External segmentation complete. Genital organs single or double. Genital pores ventral, median or submedian; cirrus, vagina, and uterine pores in a longitudinal row, in order named; genital atrium, into which cirrus and vagina open, is provided with numerous papillæ. Ovary ventral and shell gland dorsal, always median in forms with single sets of pores. Vitellogene follicles always in cortical layer. Vas deferens very sinuous, running dorsally and changing to a globular or pyriform vesicula seminalis before opening into the cirrus pouch. Testicles in the medullary layer, for the greater part outside of the longitudinal bands. The vagina, extending ventrally, crosses the uterus near its pore, and widens to a receptaculum seminis (the limits of which are not distinctly defined distally, but distinctly defined proximally) opposite the narrow and short seminal canal which unites with the oviduct to form the fertilization canal. Uterus often forms a "rosette." Eggs with operculum.

^a SYNONYM.—*Pseudophyllidea* Carus, 1863; *Bothriocephaloidea* Braun, 1903.

^b SYNONYM.—*Bothriocephalidæ* of authors.

Larval stages, for most species, unknown; adult in intestine of mammals, birds, and reptiles.

TYPE GENUS.—*Dibothriocephalus* Luehe, 1899.

Of the six genera *Dibothriocephalus*, *Duthiersia*, *Scyphocephalus*, *Bothridium*, *Diplogonoporus*, and *Pyramicocephalus*, only two (*Dibothriocephalus* and *Diplogonoporus*, for key see p. 11) are reported for man. See also *Sparganum*, p. 83.

Genus DIBOTHRIOCEPHALUS Luehe, 1899.

GENERIC DIAGNOSIS.—*Dibothriocephalinae* (p. 14): Scolex more or less elongate, groove-like suckers not highly developed. Neck present or absent. Genital organs in single series. Testicles and vitellogene glands in the lateral fields, occasionally anterior and posterior in the median field, in some cases reaching the median line. Vitellogene follicles, at least in part, situated between inner and outer longitudinal muscle layer. Uterus a long canal, in middle field, forming a rosette. Parasitic in man, felines, canines, pennipedia, and water birds. Larva (plerocercoid) in fish.

TYPE SPECIES.—*Dibothriocephalus latus* (Linnæus, 1758) Luehe, 1899.

The 2 species of this genus which occur in man may be distinguished by the following key:

KEY TO THE SPECIES OF DIBOTHRIOCEPHALUS REPORTED FOR MAN.^a

- Head oblong; strobila 2 to 10 meters or more long, 20 mm. in maximum breadth; with 3,000 to 4,000 segments; the broad tapeworm.....*D. latus* (p. 15)
 Head cordiform; strobila 80 to 115 cm. long, not over 8 mm. broad; 400 to 660 segments present; found in Greenland; rare in man*D. cordatus* (p. 19)

The Broad Tapeworm—DIBOTHRIOCEPHALUS LATUS^b (Linnæus, 1758)
 Luehe, 1899.

[Figs. 1 to 13.]

^a WARD'S NEW BOTHRIOCEPHALID TAPEWORM, 1906.—Since this bulletin was sent to press, Ward has announced that he has obtained specimens of an apparently undescribed bothriocephalid tapeworm, taken from a six-year-old child, in the prairie region of North America; the patient had eaten raw fish. Details will be published later by Ward.

^b SYNONYMS.—*Tænia lata* Linnæus, 1758a; *T. vulgaris* Linnæus, 1758a; *T. grysea* Pallas, 1761; *T. membranacea* Pallas, 1781; *T. tenella* Pallas, 1781; *T. lata hominis* Bloch, 1782a; *T. vulgaris* vel *grisea* vel *membranacea* Fischer, 1789a; *T. lata* vel *candida* Fischer, 1789a; *T. tenella* Fischer, 1789a; *T. vulgaris* Gmelin, 1790a; *Tenia inermis humana* Brera, 1802a; *Tænia inermis* Weber's Brera, 1803a [not Moquin-Tandon, 1860]; *Halysis lata* (Linnæus, 1758) Zeder, 1803a; *H. membranacea* (Pallas, 1781) Zeder, 1803a; *Tænia humana inermis* Rudolphi, 1810a; *Botryocephalus hominis* Lamarck, 1816; *Bothriocephalus latus* (Linnæus, 1758) Bremser, 1819a; *Dibothrium latum* (Linnæus, 1758) Diesing, 1850a; *Bothriocephalus cristatus* Davaine, 1873a; *Tænia fenestrata* Colin, 1876a; *Botriocephalus vulgaris cristatus* (Davaine, 1873) Grassi, 1880a; *B. vulgaris latus* (Linnæus, 1758) Grassi, 1880a; *B. vulgaris tenellus* (Pallas, 1781) Grassi, 1880a; *B. tenellus* (Pallas, 1781) Grassi, 1880a; *Bothriocephalus latus tenellus* (Pallas, 1781) Guzzardi Asmundo, 1885a; *B. latissimus* Burgnion, 1886; *B. dorpatensis* Thoma in Kuechenmeister, 1886c; *B. balticus* Thoma in Kuechenmeister, 1886c; *Bothriocephalus latus fenestratus* Maggiora, 1891; *B. fenestratus* Maggiora, 1891; *Dibothriocephalus latus* (Linnæus, 1758) Luehe, 1899; *D. cristatus* (Davaine, 1873) Luehe, 1899.

BIBLIOGRAPHY.—For zoological discussion, see Leuckart, 1886, 864–929, figs. 357–393; for medical literature, see Stiles & Hassall, Index-Catalogue of Medical and Veterinary Zoology.

SPECIFIC DIAGNOSIS.—*Dibothriocephalus* (p. 15): Strobila attains 2 to 10 [or 20?] meters in length and 20 mm. in width; usually grayish yellow to brown in color; composed of 3,000 to 4,200 segments usually broader than long, especially in anterior two-thirds of strobila; posterior segments become quadrate or even longer than broad, like the segments of *Tænia*. Head oblong, almond shaped, 2 to 3 mm. long, 0.7 to 1 mm. broad, with groove-like suckers. Neck long, or short, thin. Gravid segments

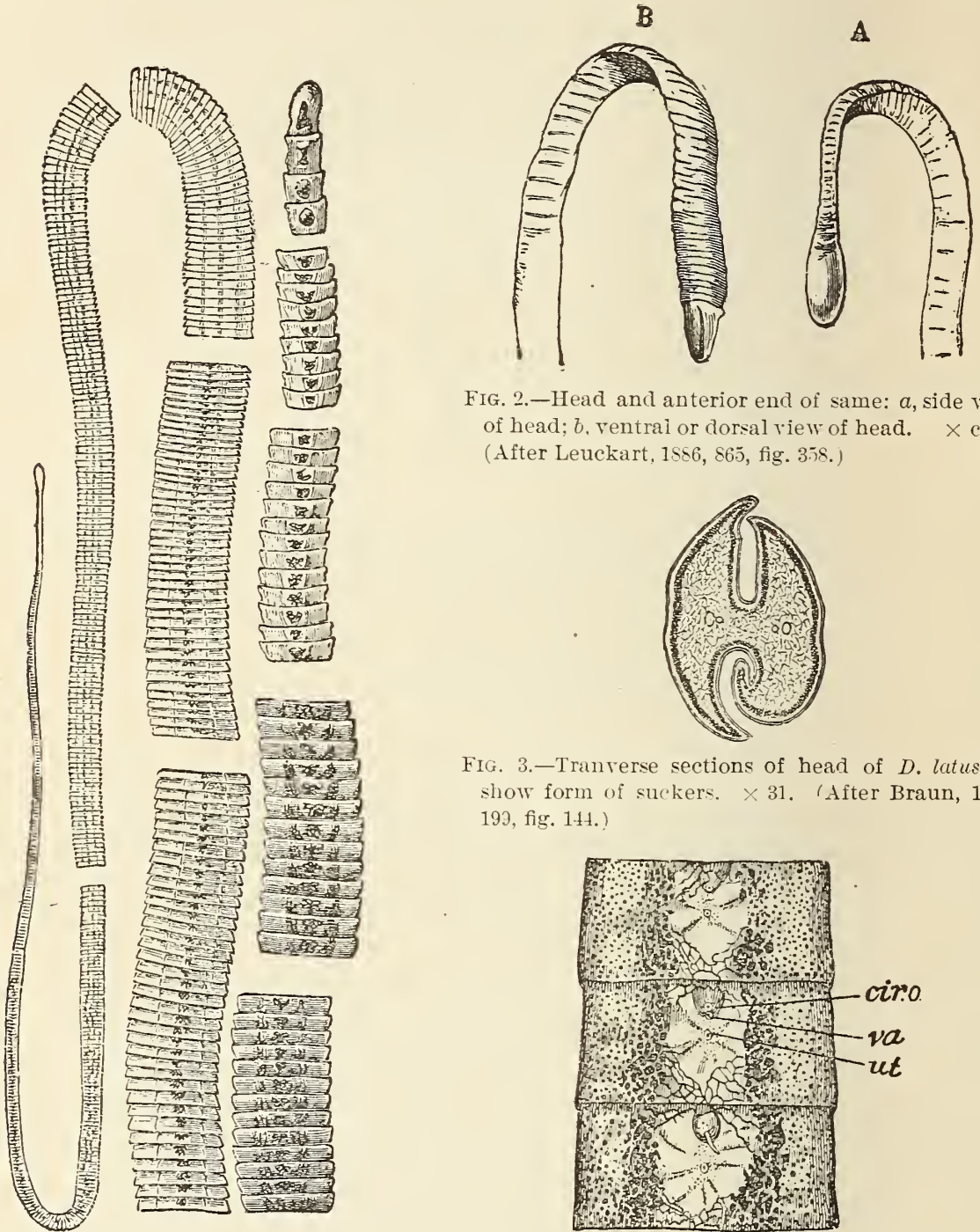


FIG. 1.—Strobila of the Broad Tapeworm (*Dibothriocephalus latus*); note the row of rosettes (uterus) in the median line. Natural size. (After Leuckart, 1886, 865, fig. 357.)

FIG. 2.—Head and anterior end of same: *a*, side view of head; *b*, ventral or dorsal view of head. \times ca. 8. (After Leuckart, 1886, 865, fig. 358.)

FIG. 3.—Transverse sections of head of *D. latus*, to show form of suckers. \times 31. (After Braun, 1903, 193, fig. 144.)

FIG. 4.—Ventral view of three segments of *D. latus*: *cir.o.*, male pore; *va.*, vagina; *ut.*, opening of uterus, through which eggs escape; in the third segment the cirrus (penis) is extruded. Enlarged. (After Eschricht, from Railliet, 1893a, 316, fig. 205.)

usually measure 2 to 4 mm. long by 10 to 12, even 20 mm. broad; they gradually lose their eggs, so that posterior segments may be entirely devoid of them. Uterus with 4 to 6 loops each side of the median line. Calcareous corpuscles few. Eggs may appear 600 segments back of the head; they are brownish, elliptical, with a small operculum, and measure 68 to 71 μ by 44 to 45 μ ; laid during segmentation. Segments break loose in chains instead of singly.

Plerocercoid: In muscles of fish.

HABITAT.—Adult in intestine of man, dogs, cats, foxes; larva a plerocercoid in various fishes—common pike (*Esox lucius*), ling (*Lota lota*), perch (*Perca fluviatilis*), several members of the salmon family (*Salmo umbla*, *S. trutta*, *S. lacustris*, *Thymallus vulgaris*, *Coregonus laveratus*, *C. albula*, *Onchorhynchus kisutch*, and perhaps *Salmo salar*).

GEOGRAPHIC DISTRIBUTION.—Reported particularly from the Baltic provinces, French Switzerland, and Japan. From these districts it has spread into France, Italy, Germany, Russia, Finland, Sweden, Denmark, Holland, Belgium, and Ireland; it is also reported for Madagascar, and a few cases are known for the United States. In some localities 5 to 20 per cent of the inhabitants are alleged to harbor the worm.



FIG. 5.—Longitudinal, sagittal section of similar segment, showing the relative position of the three genital pores. Enlarged. (After Leuckart, 1886, 877, fig. 363.)



FIG. 6.—Transverse section of a segment at height of cirrus-pouch, to show the relative position of organs. $\times 10$. (After Leuckart, 1886, 878, fig. 364.)



FIG. 7.—Dorsal view of genital organs: *ov.*, ovary; *s. g.*, shell gland; *t.*, testicles; *ut.*, uterus; *v. d.*, vas deferens. $\times 20$. (After Leuckart, 1886, 882, fig. 365.)

SPECIAL MEDICAL SIGNIFICANCE.—A number of patients exhibit anemia, known as *Bothriocephalus*-anemia. Anemia is more likely to develop in case of infection with this parasite than it is with any other tapeworm.

Upon infection the worm grows at a rate of 31 to 32 segments per day, about 2.2 to about 9 cm. in total length; eggs may be found in the feces 24 days after infection.

PREVENTION.—Eat no raw or undercooked fish.

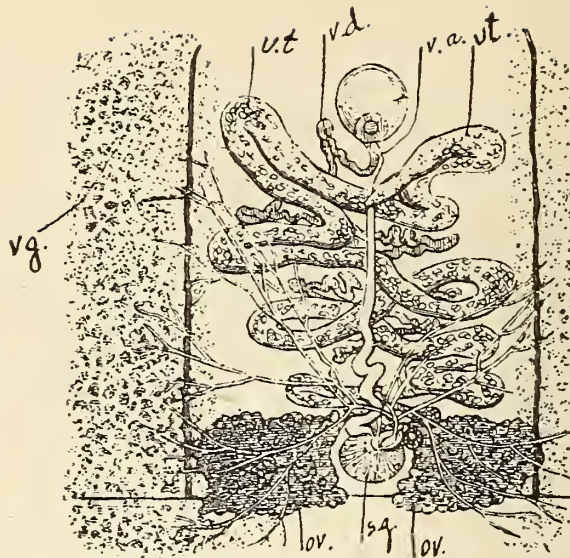


FIG. 8.—Ventral view of same, same lettering as in fig. 7: *va.*, vagina; *v. g.*, vitellogene glands. $\times 20$. (After Leuckart, 1886, 884, fig. 366.)

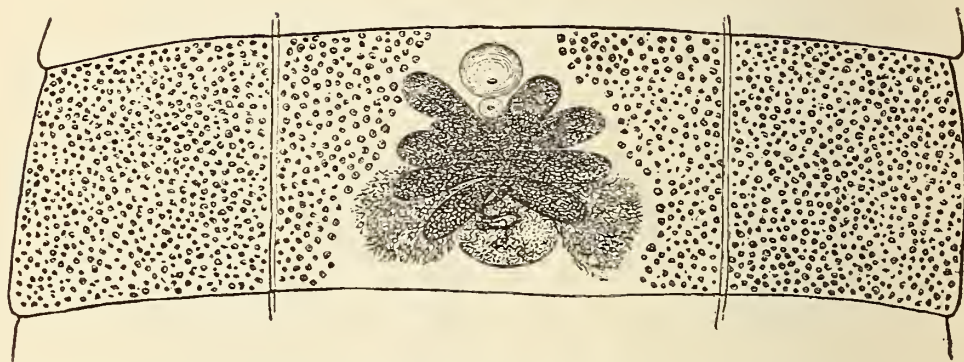
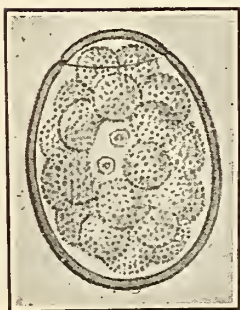
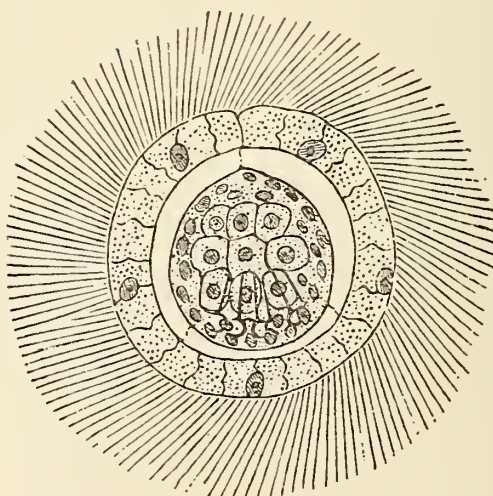


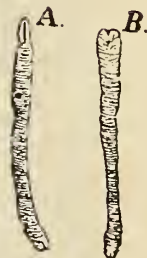
FIG. 9.—Gravid segment of *D. latus*, showing the rosette uterus in the median line. $\times 6$. (After Leuckart, 1886, 887, fig. 368.)



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FIG. 10.—Egg of *D. latus*. $\times 400$. (After Looss, 1905, pl. 9, fig. 14.)

FIG. 11.—Free swimming embryo (onchosphere) of *D. latus*. Greatly enlarged. (After Schauinsland; from Braun, 1903, 200, fig. 147.)

FIG. 12.—Two larvæ (plerocercoids) of *D. latus*: *a*, with extruded head; *b*, with retracted head; from a fish (*Esox lucius*). (After Braun, 1903, 201, fig. 149.)

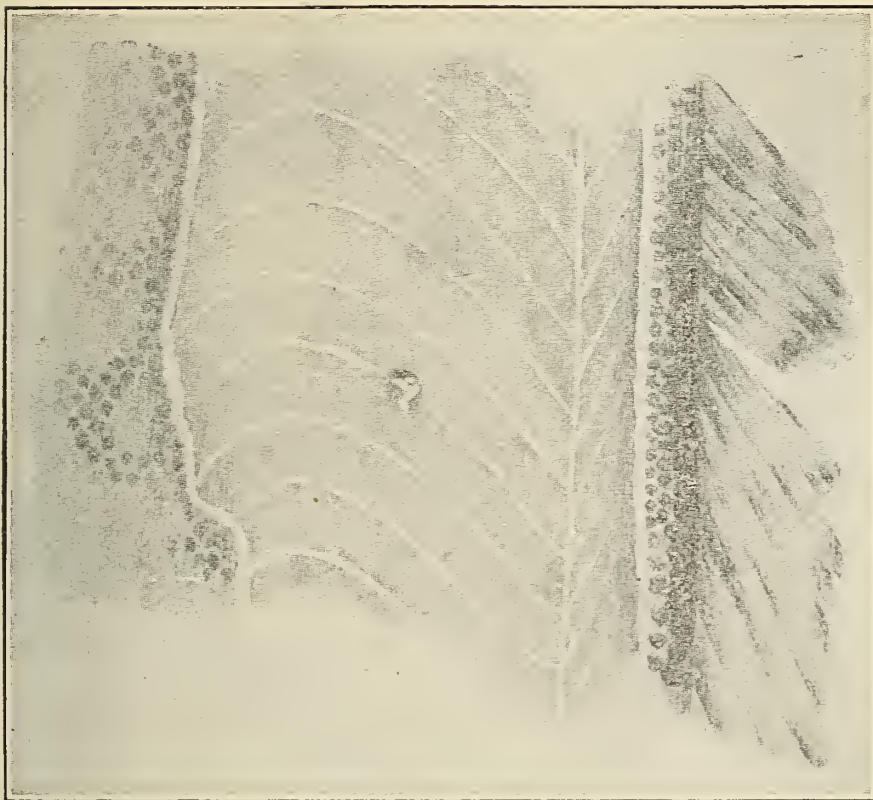


FIG. 13.—A portion of the body wall of a fish (*Lota lota*), containing a plerocercoid (infecting stage) of *D. latus*. Natural size. (After Braun, 1903, 201, fig. 150.)

The Cordate Tapeworm—*DIBOTHRIOCEPHALUS CORDATUS*^a (Leuckart, 1863) Luehe, 1899.

[Figs. 14 to 20.]

SPECIFIC DIAGNOSIS.—*Dibothriocephalus* (p. 15): Similar to *D. latus*, but smaller, attaining 80 to 115 cm. in length and composed of 400 to 660 segments. Head short, broad (dorso-ventrally), heart shape or arrow-head shape, 2 by 2 mm.; suckers deep in forward half. Neck absent, segmentation beginning immediately at the head, the segments rapidly becoming broader, so that the cephalic end is more or less lanceolate; only about 50 immature segments present, genital pores and genital primordia visible in specimens 80 mm. long; at 3 cm. from head, segments attain 7 to 8 mm. in breadth and become mature; mature segments 3 to 4 mm. long, but may contract to 1.3 mm.; terminal segments nearly square 5 to 6 mm. Dorso- and ventro-median lines grooved. Calcareous corpuscles 28 to 30 μ , numerous. Longitudinal muscles very well developed. Cirrus-pouch 0.6 by 0.43 mm. Uterus with 6 to 8 lateral loops each side; eggs ellipsoid 75 to 80 by 50 μ .

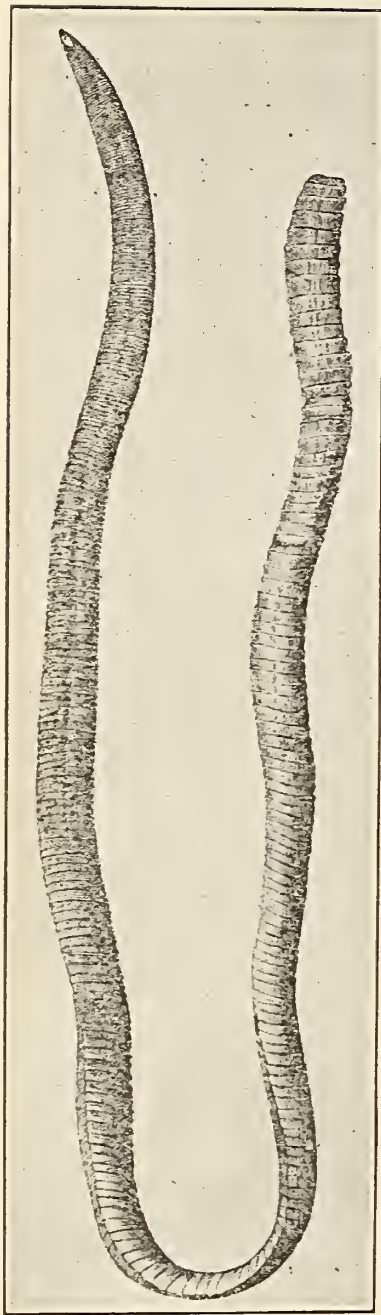
Plerocercoid.—Unknown.

HABITAT.—Adults in dogs (*Canis familiaris*) in Godhavn, North Greenland; bearded seal (*Erignathus barbatus*), Disco Island; walrus (*Odobenus rosmarus*). One case found in man in Greenland. Larva probably in fish.

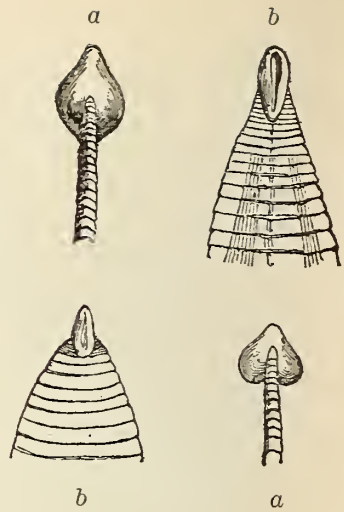
MEDICAL SIGNIFICANCE.—Unknown at present; possibly accidental in man.

^aSYNONYMS. — *Bothriocephalus cordatus* Leuckart, 1863; *Dibothrium cordatum* (Leuckart, 1863) Diesing, 1863a; *Botriocephalus cordatus* (Leuckart, 1863) Grassi, 1880a.

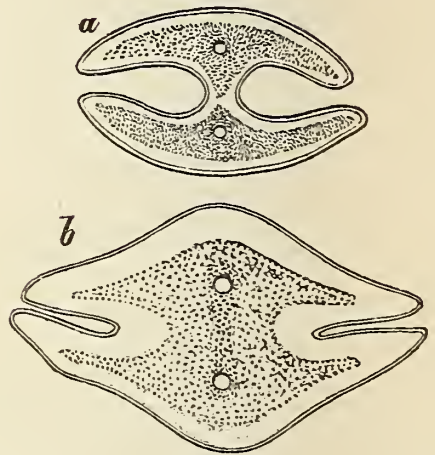
BIBLIOGRAPHY.—For zoological discussion, see Leuckart, 1886, 930–941, figs. 394–401.



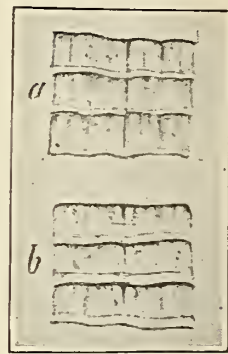
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FIG. 14.—*Dicrocoelium cordatus* from man. Natural size. (After Leuckart, 1886, 934, fig. 397.)

FIG. 15.—Head and anterior portion of *D. cordatus*: *a*, lateral view; *b*, dorsal and ventral view. $\times 5$. (After Leuckart, 1886, 931, fig. 394.)

FIG. 16.—Transverse sections of head to show depth of suckers: *a*, in front of middle of head; *b*, back of middle of head. \times ca. 10. (After Leuckart, 1886, 937, fig. 400.)

FIG. 17.—Three segments of *D. cordatus*: *a*, dorsal view; *b*, ventral view. $\times 2$. (After Leuckart, 1886, 934, fig. 399.)

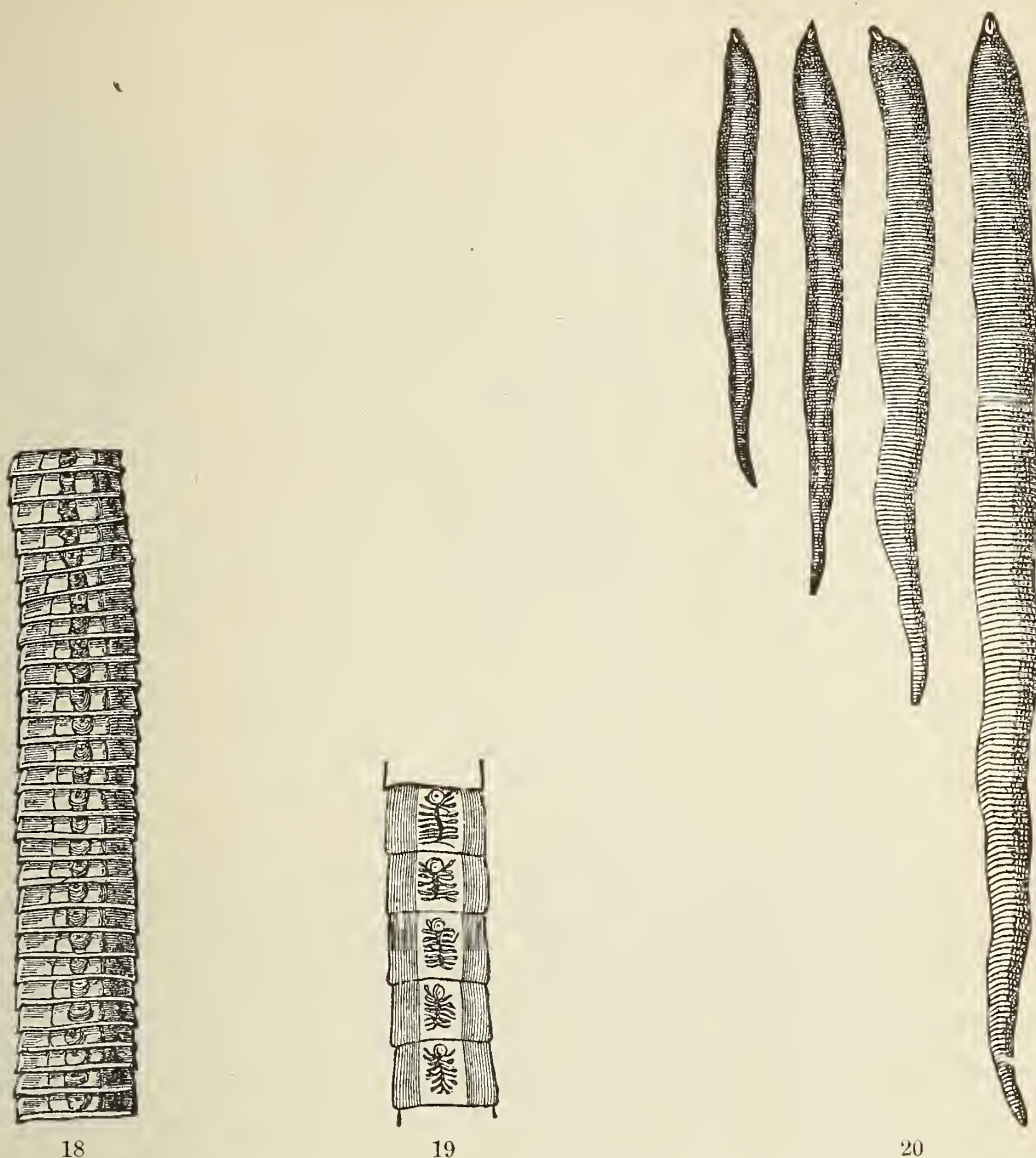


FIG. 18.—Portion of strobila of *D. cordatus*; note rosette uterus in median line. Natural size. (After Leuckart, 1886, 931, fig. 395.)

FIG. 19.—Five segments of *D. cordatus*, showing the form of the uterus. Natural size. (After Leuckart, 1886, 931, fig. 396.)

FIG. 20.—Four young specimens of *D. cordatus*. Natural size. (After Leuckart, 1886, 939, fig. 401.)

Genus DIPLOGONOPORUS^a Lœnnberg, 1892.

GENERIC DIAGNOSIS.—*Dibothriocephalinæ* (p. 14): Scolex short, with two strong groove-like suckers. Neck absent. Proglottids short and broad. In each segment, two sets of genital organs, otherwise like *Dibothriocephalus*. In each segment may be recognized: median field, two uterine fields, two lateral fields. Genital pores (cirrus, vaginal, uterine) in longitudinal row in uterine field; vitellogene glands and testicles in lateral and median fields. Vitellogene follicles between inner and outer longitudinal muscles. Uterus forms rosette. Parasites in man and whales.

TYPE SPECIES.—*Diplogonoporus balænopterae* Lœnnberg, 1892.

^aSYNONYMS.—*Bothriocephalus* (*Diplogonoporus*) Lœnnberg, 1892; *Diplogonoporus* Lœnnberg, 1892, (type *balænopterae*); *Krabbea* Blanchard, 1894i (type *grandis*).

The Japanese Double-pored Tapeworm—*DIPLOGONOPORUS GRANDIS* ^a
(Blanchard, 1894) Luehe, 1899.

[Figs. 21 to 27.]

SPECIFIC DIAGNOSIS.—*Diplogonoporus*: Strobila attains to 10 meters in length, 10 to 25 mm. in breadth; number of segments unknown. Head undescribed. Neck undescribed. Genital pores open in longitudinal genital grooves. Gravid segments con-

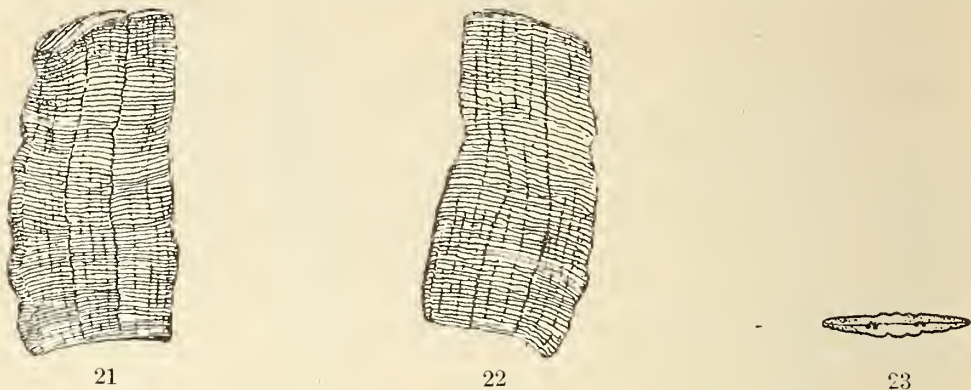


FIG. 21.—Dorsal view of a portion of the strobila of the double-pored large tapeworm (*Diplogonoporus grandis*) of man. Natural size. (After Ijima & Kurimoto, 1894a, fig. 1.)

FIG. 22.—Ventral view of same. (After Ijima & Kurimoto, 1894a, fig. 2.)

FIG. 23.—Transverse section of same. (After Ijima & Kurimoto, 1894a, fig. 3.)

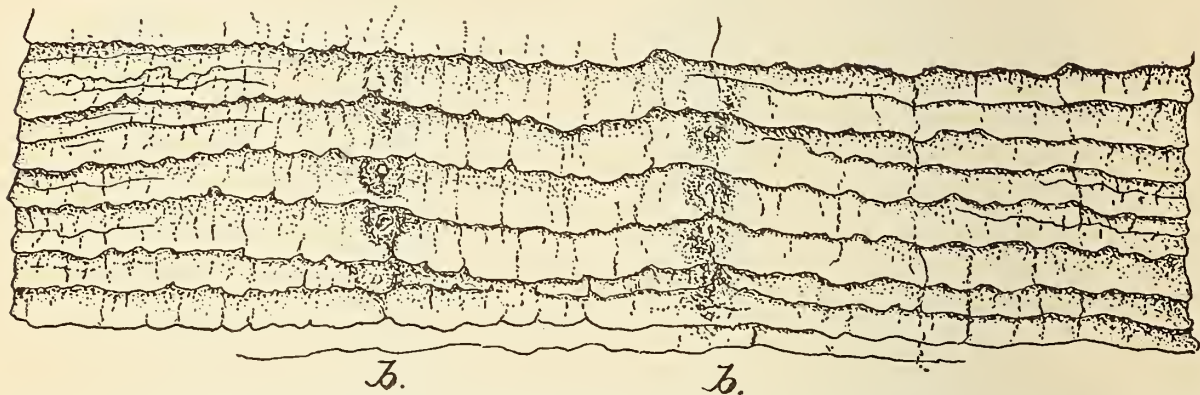


FIG. 24.—Ventral view of a portion of the strobila, showing two rows of genital pores, with partially extruded cirri. $\times 10$. (After Ijima & Kurimoto, 1894a, fig. 6.)

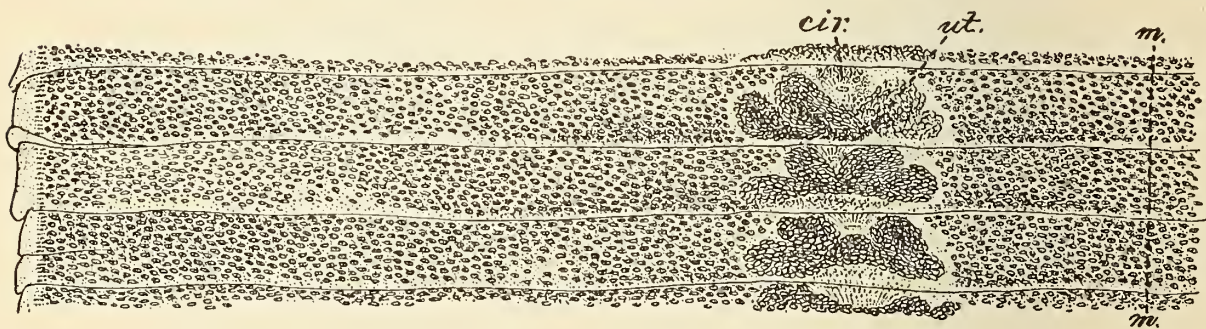


FIG. 25.—Ventral view of lateral half of same: *m.*, median line of segment; *cir.*, cirrus; *ut.*, uterus; the numerous dot-like bodies on either side of the uteri represent the yolk glands. $\times 20$. (After Ijima & Kurimoto, 1894a, fig. 7.)

tracted in alcohol to 0.45 mm. long, by 14 to 16 mm. broad. Uterus with but few (about 2) loops each side. Eggs brownish, rather opaque, 63μ long by 48 to 50μ broad.

Plerocercoid: Unknown.

HABITAT.—In intestine of man, Japan; larva unknown, in all probability in fish.

^aSYNONYMS.—*Bothriocephalus* sp. Ijima & Kurimoto, 1894; *Krabbea grandis* Blanchard, 1894i.

BIBLIOGRAPHY.—See Stiles & Tayler, 1902a, 43–47, figs. 22–28, for medical and zoological summary.

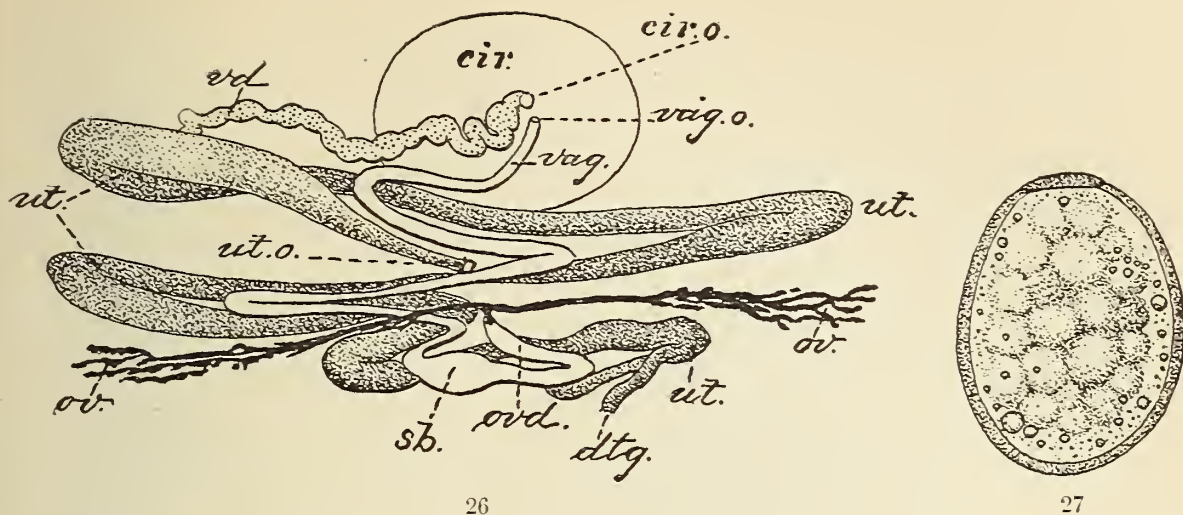


FIG. 26.—Partially diagrammatic representation of a left set of main genital ducts as seen in ventral view: *cir.*, cirrus; *cir. o.*, cirrus opening; *dtg.*, yolk duct; *ov.*, ovary; *ord.*, oviduct; *sb.*, receptaculum seminis; *ut.*, uterus; *ut. o.*, uterine pore; *vag.*, vagina; *vag. o.*, vaginal opening; *v. d.*, vas deferens. $\times 150$. (After Ijima & Kurimoto, 1894a, fig. 10.)

FIG. 27. An egg of *D. grandis*, taken from the uterus. $\times 440$. (After Ijima & Kurimoto, 1894a, fig. 9.)

MEDICAL SIGNIFICANCE.—Apparently similar to *Dibothriocephalus latus*.

Superfamily TÆNIOIDEA.^a

SUPERFAMILY DIAGNOSIS.—*Cestoda*: Scolex with four cup-shaped suckers; between these may be an apical rostellum of various forms; suckers and rostellum may be armed with hooks or unarmed. In exceptional cases a pseudoscolex develops. Neck present or absent. Segmentation nearly always complete; mature segments usually do not escape until completely developed. Uterus without special pore. Cirrus and vagina usually open on margin, exceptionally on ventral surface. Genital organs usually in single series; in some cases in double series, complete or incomplete. Testicles in medullary layer, usually numerous. Ovary more or less bilobed. Vitellogene gland usually single, and distal of ovary at distal margin of the segment, seldom anterior of ovary; shell-gland between ovary and vitellogene gland. Eggs without operculum; onchosphere with one or several membranes. Bladder worm stage in vertebrates or in invertebrates. Adults in intestine of vertebrates, especially mammals

TYPE AND ONLY FAMILY.—*Tæniidæ*.

Family TÆNIIDÆ^b Ludwig, 1886.

FAMILY DIAGNOSIS.—Same as diagnosis of superfamily *Tænioidea*.

This family is divided into the subfamilies *Mesocestoidinæ*, *Acoleinæ*, *Amabiliinæ*, *Tetrabothriinæ*, *Anoplocephalinæ*, *Dipylidiinæ*, *Davaineinæ*, and *Tæniinæ*; three of these (*Dipylidiinæ*, *Davaineinæ*, and *Tæniinæ*, for key see p. 11) are represented among the parasites of man.

Subfamily TÆNIINÆ^c Stiles, 1896.

SUBFAMILY DIAGNOSIS.—*Tæniidæ*: Usually large species; gravid segments usually considerably longer than broad. Scolex with rostellum and usually with double row

^a SYNONYM.—*Cyclophyllidea*.

^b SYNONYM.—*Tæniadæ*.

^c SYNONYMS.—*Tæniea* Goldberg, 1855a; *Cystotæniæ* Claus, 1876; *Tænianæ* Railliet, 1896.

of hooks; in exceptional cases rostellum is developed into an apical sucker, the armature (hooks) becoming lost. Genital pores irregularly alternate. Testicles usually very numerous, in lateral portions of median field. Ovary, shell gland, and vitellogene gland in distal half of middle zone; uterus with median stem, which develops lateral branches; the latter afterwards suppress the genital glands. Of the four longitudinal excretory canals, usually only the ventral remain visible in the gravid segments. Egg shell thin, with or without filaments, and usually becomes destroyed; embryonal shell (embryophore) thick, radially striated.

Bladder worm stage, a cysticercus, *cœnurus*, or *echinococcus*, in herbivorous or omnivorous animals; adults in carnivorous animals.

TYPE GENUS.—*Tænia* Linnæus, 1758.

This subfamily contains two genera, represented among the parasites of man, namely, *Tænia* and *Echinococcus*; the former is represented among the intestinal parasites of man, the latter (see p. 75) among the somatic parasites of man.

Genus TÆNIA ^a Linnæus, 1758.

GENERIC DIAGNOSIS.—*Tæniinæ* (p. 23): In general, same as diagnosis of subfamily *Tæniinæ*; larval stage a cysticercus. Adults in carnivorous mammals; larval stage chiefly in herbivorous and omnivorous mammals.

TYPE SPECIES.—*Tænia solium* Linnæus, 1758.

This genus is divided into several subgenera, which some authors have recognized, not entirely without reason, as entitled to full generic rank. These subgenera—or, if one prefers, genera—may be distinguished as follows:

KEY TO THE SUBGENERA (OR GENERA) OF TÆNIA.

(For forms reported for man follow roman type.)

1. Segments always more than 10, usually more than 100; lateral uterine branches distinct; vitellogene gland triangular, with one side parallel to posterior margin of segment; larval stage never forms brood capsules 2
 Strobilla composed of head and three segments, only one of which is gravid at a time; lateral uterine branches often quite indistinct; vitellogene gland globular; larval stage an *echinococcus*, which forms brood capsules inside of which the scolices develop..... *Echinococcus* (p. 75)
2. Head with distinct rostellum armed with double crown of hooks..... 3
 Rostellum rudimentary; hooks small and become lost very early, so that head appears unarmed, the crown of hooks being replaced by a structure known as the "apical" or "fifth" sucker; larva a cysticercus..... *Tæniarhynchus* (p. 26)
3. Larva a cysticercus, namely, a small bladder worm with one scolex. *Tænia* (p. 36)
 Larva a *cœnurus*, namely, a bladder worm with numerous heads, but without brood capsules *Multiceps*.^b

^a SYNONYMS.—See synonymy of subgenera *Tænia*, p. 36, and *Tæniarhynchus*, p. 26.

^b Not represented among the parasites of man. *Multiceps* Gœze, 1782; *Polycephalus* Zeder, 1800; *Cœnurus* Rupolphi, 1808; *Polycephops* Rafinesque, 1815; *Cœnurus* Cuvier, 1825a; *Canurus* Goodsir, 1844g.

All of the forms found in man are usually referred to simply as members of the genus *Tænia*, as *Tænia solium*, *Tænia saginata*, etc.

Difficulty is occasionally experienced by physicians in determining tapeworms when they have only a part of the parasite for examination. To meet the difficulties which thus arise, the following key is prepared:

KEY TO THE SPECIES^a OF *TENIA* FOUND IN MAN.

(For species known to occur in man in the United States, follow roman type.)

1. Strobila 2
 - Head 3
 - Segments 7
 - Mature segments (namely, with genital glands) 8
 - Gravid segments (namely, with eggs) 12
 - Source of infection 15
2. Strobila attains:
 - 2 to 3.5, rarely 6 to 8 meters in length; head armed; cosmopolitan ... *T. solium* (p. 37)
 - 4 to 10 meters in length (*T. saginata* and *T. confusa*) 1
 - 1.4 meters in length; head unarmed; Africa *T. africana* (p. 32)
 - unknown length; original immature specimen measured 70 mm. long; head unarmed; Asiatic Russia *T. hominis* (p. 36)
 - 0.5 to 2 meters in length; head armed *T. pisiformis* (p. 41)
 - 0.15 to 0.6 meters in length; head armed *T. teniæformis* (p. 43)
3. Head:
 - armed with hooks (subgenus *Tænia*) 4
 - unarmed (subgenus *Tæniarhynchus*) 5
 - unknown; see also 1 *T. confusa* (p. 44)
4. Rostellum:
 - short, armed with 24 to 32 hooks; see also 2 *T. solium* (p. 37)
 - rather powerful, armed with 34 to 48 hooks; see also 2 *T. pisiformis* (p. 41)
 - very prominent, armed with 26 to 52 hooks; see also 2 *T. teniæformis* (p. 43)
5. A circular ring surrounds head back of suckers, which are directed postero-anteriorly; Asiatic Russia *T. hominis* (p. 36)
- No such circular ring present 6
6. Head rather cuboid, 1.5 to 2 mm. in diameter; suckers 0.7 to 0.8 mm. in diameter *T. saginata* (p. 27)
- Head rather small, 1.38 mm. broad, 1.03 mm. thick, 0.47 mm. long; suckers 0.63 mm. in diameter; Africa *T. africana* (p. 32)
7. Segments:
 - become longer than broad (*T. solium*, *T. pisiformis*, *T. crassicollis*, *T. saginata*, *T. confusa*) 1
 - become longer than broad only in last 100 proglottids *T. saginata* (p. 27)
 - become longer than broad in last half of worm *T. solium* (p. 37)
 - are longer than broad in nearly entire worm *T. confusa* (p. 44)
 - always broader than long; Africa; see 1 *T. africana* (p. 32)
 - unknown; Asiatic Russia; see 1 *T. hominis* (p. 36)

^a*T. pisiformis* and *T. teniæformis* are included in this table, although there are doubts regarding their occurrence in man.

8. Mature segments measure:
- 2.5 to 3 mm. long, 4.5 to 5 mm. broad (*T. solium*) 9
 - 4 to 4.5 mm. long, 3.5 to 4.5 mm. broad (*T. confusa*)..... 9
 - 4 to 6 mm. long, 8 to 10 mm. broad (*T. saginata*) 9
 - 2 mm. long by 7 mm. broad (*T. africana*)..... 9
 - unknown; Asiatic Russia (*T. hominis*) 3
9. Ovary divided into 2 portions, right and left of median line..... 10
- Ovary divided into 3 portions, 2 being on pore side of the segment.....
- T. solium* (p. 37)
10. Ovaries in distal half of segment..... 11
- Ovaries fan-shaped, composed of club-shaped tubes centering toward the shell gland, and occupying the 2nd and 3rd transverse fourths of segment; Africa.*
- T. africana* (p. 32)
11. Ovarian lobes:
- round; testicles 0.15 mm. in diameter.....*T. saginata* (p. 27)
 - reniform; testicles 0.089 to 0.096 mm. in diameter.....*T. confusa* (p. 44)
12. Gravid segments (as passed from anus):
- longer than broad; uterine branches more or less dichotomous..... 13
 - broader than long; 15 to 24 simple lateral uterine branches; Africa*
 - T. africana* (p. 32)
13. Gravid segments 27 to 35 mm. long, 3.5 to 5 mm. broad; uterus with 14 to 18 short, thick, lateral branches each side.....*T. confusa* (p. 44)
- Gravid segments less than 26 mm. long 14
14. Gravid segments:
- 12 to 20, rarely to 25, mm. long by 4 to 7 mm. broad; uterus with 15 to 30 slender uterine branches each side of median stem....*T. saginata* (p. 27)
 - 10 to 12 mm. long, 5 mm. broad; uterus with 7 to 14 short, thick, uterine branches each side of median stem.....*T. solium* (p. 37)
 - 10 to 17 mm. long, 4 to 6 mm. broad; uterus with 8 to 10 uterine branches each side of median stem*.....*T. pisiformis* (p. 41)
 - 8 to 10 mm. long, 5 to 6 mm. broad; uterus with about 12 uterine branches each side of median stem**T. teniæformis* (p. 43)
15. Cysticercus, known as:
- Cysticercus bovis*, lives in cattle.....*T. saginata* (p. 27)
 - C. cellulosa*, lives in swine.....*T. solium* (p. 37)
 - C. pisiformis*, lives in rabbits.....*T. pisiformis* (p. 41)
 - C. fasciolaris*, lives in rats and mice*T. teniæformis* (p. 43)
 - unknown.....*T. confusa* (p. 44)
 - unknown.....*T. africana* (p. 32), *T. hominis* (p. 36)

Subgenus TÆNIARHYNCHUS^a Weinland, 1858.

SUBGENERIC DIAGNOSIS.—*Tænia* (p. 24): Rostellum rudimentary; hooks small and disappearing early. Otherwise like *Tænia* (*Tænia*); see p. 36.

TYPE SPECIES.—*Tænia saginata* (Gœze, 1782).

Of the 3 species of this subgenus reported for man, only one (namely, *T. saginata*) is of any importance to physicians practicing in the United States.

^a SYNONYMS.—*Pentastoma* Virey, 1823, not Rudolphi, 1819a; *Tæniarhynchus* Weinland, 1858.

The Fat Tapeworm—*TÆNIA SAGINATA* ^a Goeze, 1782.

[Figs. 28 to 34.]

SPECIFIC DIAGNOSIS.—*Tænia* (*Tæniarhynchus*) (p. 26): Strobila attains 4 to 8 or 10 meters in length, greatest breadth 12 to 14 mm.; composed of about 1,300 segments. Head rather cuboid, 1.5 mm. to 2 mm. in diameter; rostellum very rudimentary, replaced by apical sucker-like structure 0.114 mm. in diameter; suckers 0.7 to 0.8 mm. in diameter, lumen 0.47 mm. Unsegmented neck present. Genital pore back of middle of lateral margin, genital cloaca 0.22 mm. deep, funnel-shaped. Sexually mature proglottids measure 4 to 6 mm. long, 8 to 10 mm. broad; vagina with or without setæ; ovary divided into two round lobes which lie distally of a transverse plane passing through genital pore; testicles 0.15 mm. in diameter; seminal vesicle absent; length of cirrus pouch 0.4 to 0.5 mm. Gravid (terminal) proglottids attain 12 to 20, rarely 25 mm. long, by 4 to 6.5 mm. broad; uterus with 15 to 35 dichotomous branches each side of and shorter than median stem. Calcareous corpuscles plentiful, attain 18 μ . Eggs globular, outer eggshell bears one or two filaments; embryophore thick, oval, transparent to dark brown, 30 to 40 μ long, 20 to 30 μ broad.

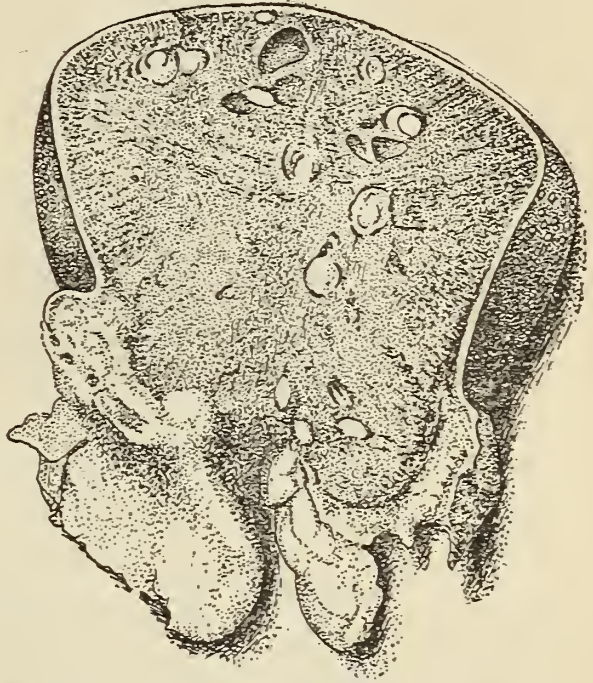


FIG. 28.—Section of a beef tongue heavily infested with beef measles, natural size. (After Stiles, 1898a, 72, fig. 68.)

^a **SYNONYMS.**—*Tænia solium* Linnæus, 1758a, pro parte; *T. cucurbitina* Pallas, 1766, pro parte; *T. cucurbitina saginata* Goeze, 1782a; *T. cucurbitina grandis saginata* Goeze, 1782a; ?*T. vulgaris* Werner, 1782 (not Linnæus, 1758a), renamed *T. deutata* Batsch, 1786a (not Nicolai, 1830); ?*T. solitaria* Leske, 1784 or 1785, pro parte (not accessible); *T. grandis* Gmelin, 1790a; *Halysis solium* (Linnæus, 1758) Zeder, 1803a, pro parte; *Pentastoma coarctata* Virey, 1823; *Tænia dentata* Nicolai, 1830; ?*T. fenestrata* delle Chiaje, 1833a; *T. lata* Pruner, 1847 (not Linnæus, 1758a); *T. tenella* Pruner, 1847 (not Pallas, 1781); *Bothriocephalus tropicus* Schmidtmueller, 1847; *Tænia mediocanellata* Kuechenmeister, 1852f; *T. mediocanellata hominis* Kuechenmeister, 1852f; *T. zittariensis* Kuechenmeister, 1852f; *T. solium mediocanellata* of Diesing, 1854b; *T. [Tæniarhynchus] mediocanellata* Kuechenmeister of Weinland, 1858; *T. solium abietina* Weinland, 1858; *T. inermis* Moquin-Tandon, 1860, and Laboulbène, 1876 (not Brera, 1803a); *T. tropica* (Schmidtmueller, 1847), Moquin-Tandon, 1860; “*T. mediocancellata* of several authors,” Moquin-Tandon, 1860; *T. capensis* Moquin-Tandon, 1860; *Tæniarhynchus mediocanellatus* (Kuechenmeister, 1852) Weinland, 1861; *Tænia megaloon* Weinland, 1861; *T. [(Cystotænia)] mediocanellata* of Leuckart, 1863; *T. lophosoma* Cobbold, 1866; *T. saginata* Goeze, 1782, of Leuckart, 1867; *T. abietina* Weinland, 1858, of Davaine, 1873a; ?*T. fusa* Colin, 1876a; ?*T. continua* Colin, 1876a; ?*T. solium fusa* Colin, 1876a; ?*T. solium continua* Colin, 1876a; *T. nigra* Davaine, 1877a; *T. algérien* Redon, 1883; *Tenia abietina* (Weinland, 1858) Guzzardi Asmundo, 1885a; *T. mediocanellata* (Kuechenmeister) Guzzardi Asmundo, 1885a; *Tænia mummificata* Guzzardi Asmundo, 1885a; *Tenia cosidetta mummificata* Guzzardi Asmundo, 1885a; *Tænia saginata abietina* Weinland of Leuckart (Hoyle), 1886; *Tenia seghettata* Bergonzini, 1886a;

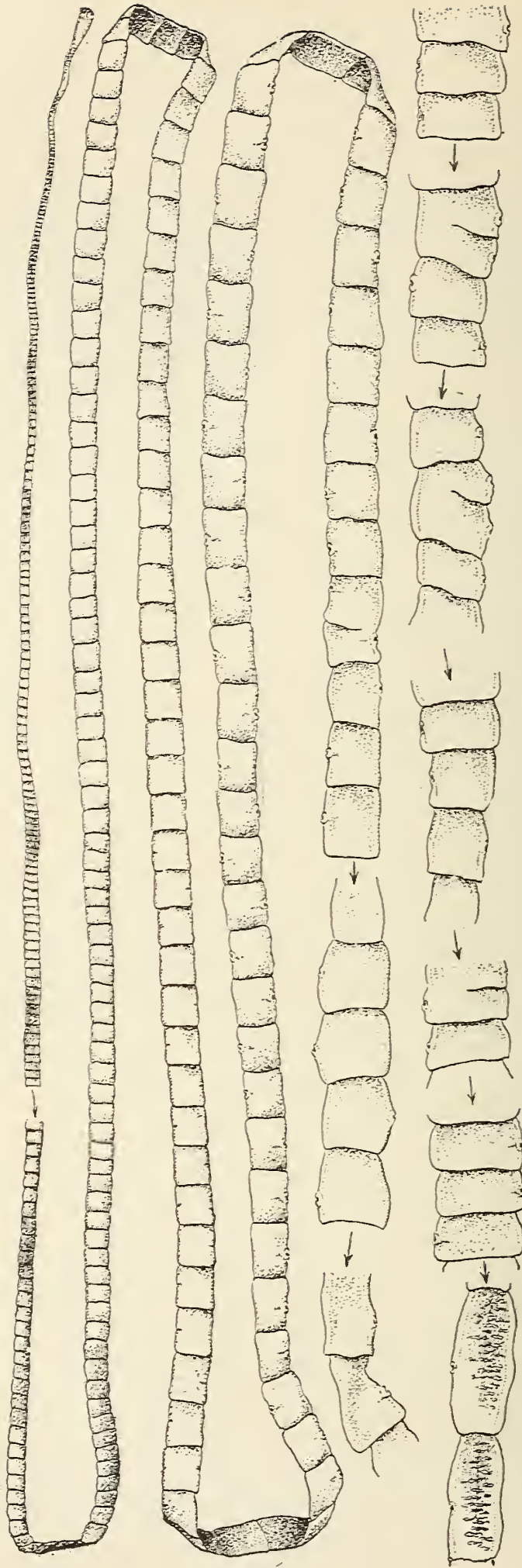


FIG. 29.—Several portions of an adult beef measles tapeworm (*Triaena saginata*) from man, showing the head on the anterior end and the gradual increase in the size of the segments, natural size. (After Stiles, '898a, 73, fig. 69.)

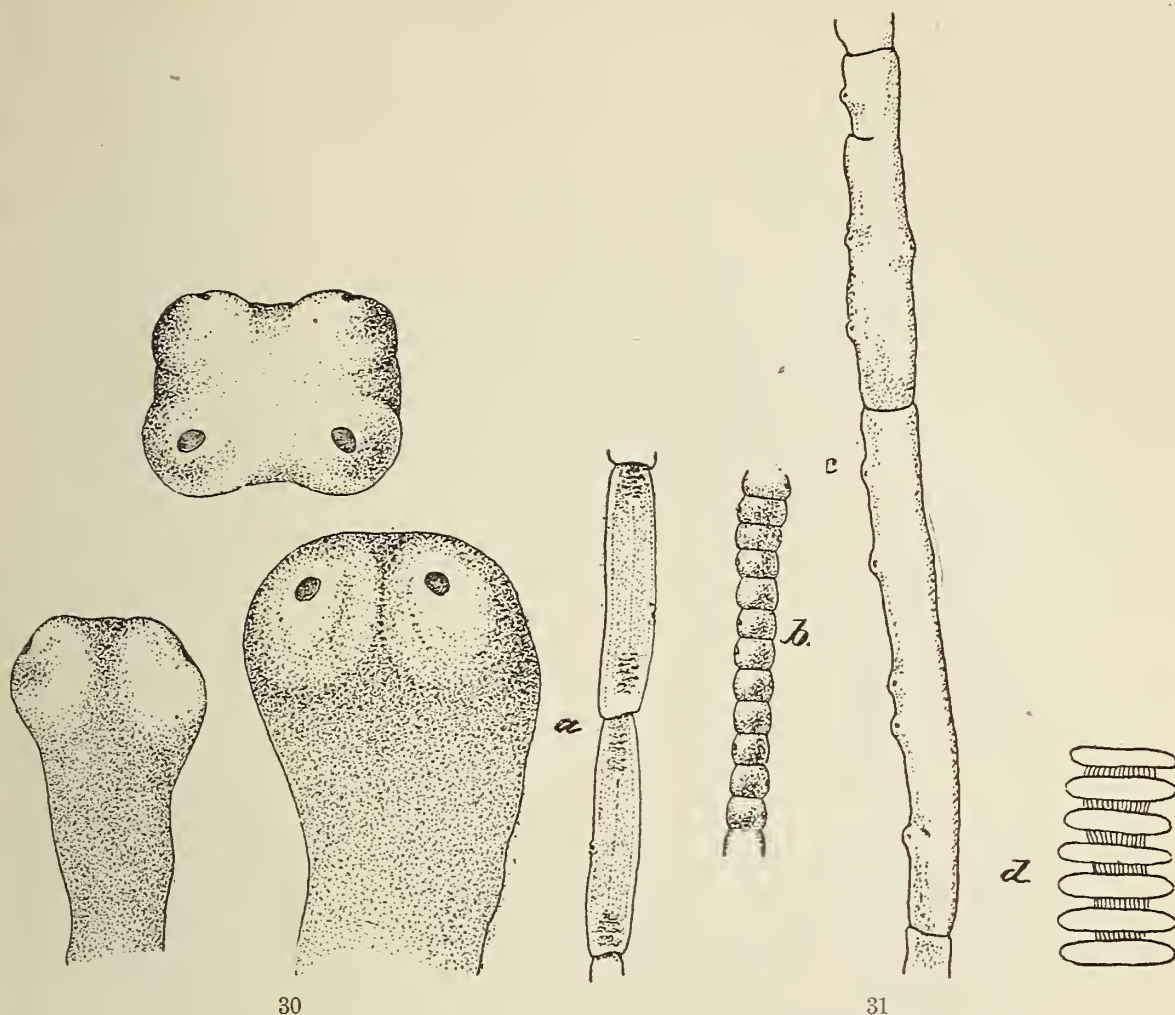


FIG. 30.—Dorsal, apex, and lateral views of the head of beef-measle tapeworm (*Taenia saginata*), showing a depression in the center of the apex. $\times 17$. (After Stiles, 1898a, 74, fig. 70.)

FIG. 31.—Segments from various strobilæ of beef-measle tapeworm (*Taenia saginata*), showing forms of proglottids which are occasionally found: *a*, elongated segments; *b*, bead-like segments; *c*, a portion of the strobila in which the segmentation is not distinct; *d*, moniliform segments (*a* and *b* after Stiles, 1898a, 75, fig. 71; *c* and *d* after Blanchard, 1894).

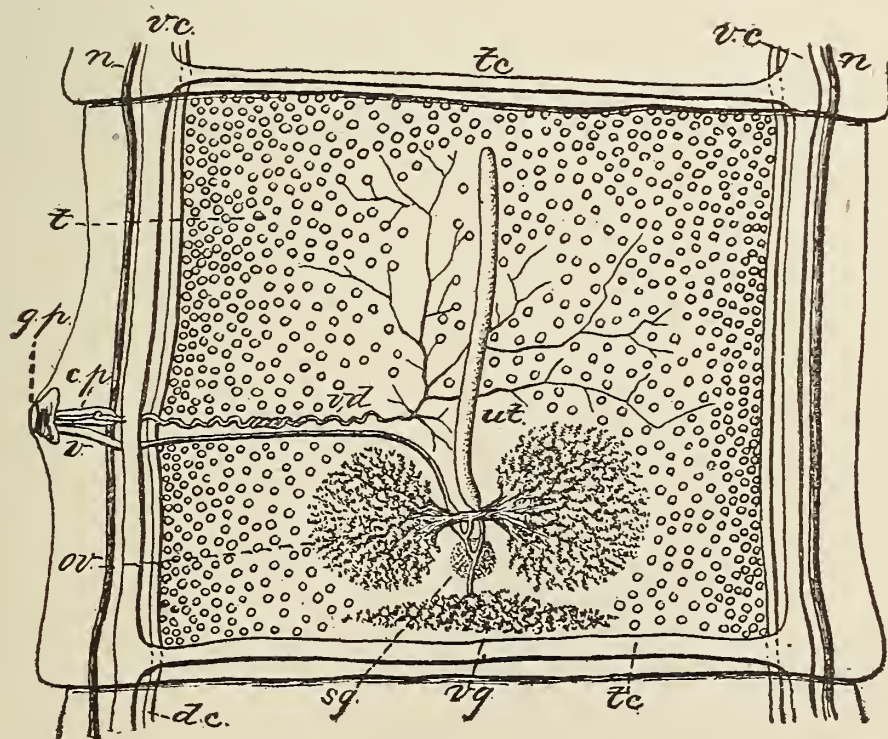


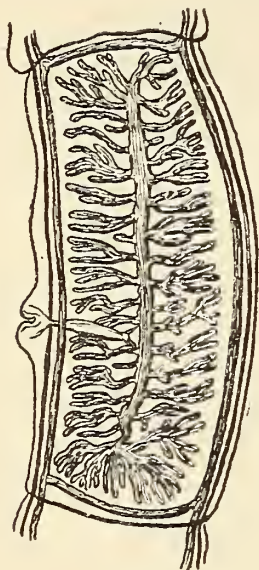
FIG. 32.—Sexually mature segment of beef-measle tapeworm (*Taenia saginata*): *c. p.*, cirrus pouch, with cirrus; *d. c.*, dorsal canal; *g. p.*, genital pore; *n.*, lateral longitudinal nerves; *ov.*, ovary; *s. g.*, shell glands; *t.*, testicles; *ut.*, median uterine stem; *v.*, vagina; *v. c.*, ventral canals connected by transverse canal, *t. c.*; *v. d.*, vas deferens; *v. g.*, vitellogene gland. Enlarged. (After Leuckart and Stiles.)

Cysticercus: *Cysticercus bovis*,^a spherical 7.5 to 10 mm. long by 3 to 5.5 mm. broad, whitish to gray with small yellow spot due to the invaginated head; no hooks present; the bladder contains but little fluid. This stage requires about 3 to 6 weeks for its development from the onchosphere.

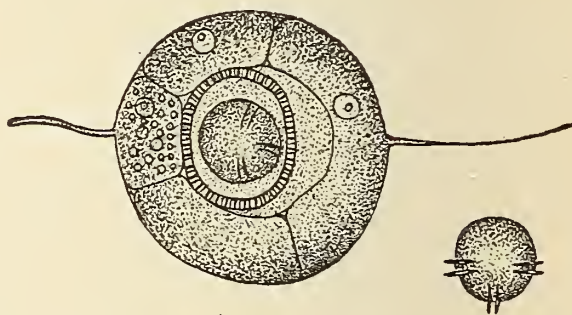
HABITAT.—Adult known only for man. *Cysticercus* found in muscles, especially tongue and masseters, of cattle (*Bos taurus*); also reported for Rocky Mountain “antelope” (*Antilocapra americana*), giraffe (*Giraffa camelopardalis*), and lama (*Auchenia llama*).

GEOGRAPHIC DISTRIBUTION.—More or less cosmopolitan.

SPECIAL MEDICAL SIGNIFICANCE.—The most common of the large tapeworms, except in certain districts where the broad tapeworm



33



34

FIG. 33.—Gravid segment of beef-measle tapeworm (*Tenia saginata*), showing lateral branches of the uterus. Enlarged. (After Stiles, 1898a, 77, fig. 73.)

FIG. 34.—Egg of beef-measle tapeworm (*Tenia saginata*), with thick eggshell (embryophore), containing the six-hooked embryo (onchosphere), enlarged. (After Leuckart.)

abounds. It is not so dangerous as *T. solium*, as there is no danger of autoinfection with *cysticercosis* (see p. 68); anemia is more likely to develop with this species than with *T. solium*, but less likely than with *Dibothriocephalus latus*; it is more difficult to expell than are the other large species.

PREVENTION.—Meat inspection; cooking of beef, especially of tongue and masseter muscles; cold storage of beef for 21 days after killing. A person with this tapeworm should never defecate in fields used for pasturing cattle.

SUBSPECIES AND VARIATIONS.—Occasionally variations, monstrosities, and pathological specimens of this species have been found and

Tenia inermis fenestrata Maggiora, 1891; *T. perforata* Maggiora, 1891; *T. algeriana* Pepper, 1894; *T. algeriensis* Braun, 1894a.

BIBLIOGRAPHY.—For zoological discussion see Leuckart, 1880, 513–616, figs. 237–273; for medical literature see Stiles & Hassall, Index-Catalogue of Medical and Veterinary Zoology.

^aSYNONYMS.—*Cysticercus tæniæ mediocanellatæ* Leuckart, 1863; *C. bovis* Cobbold, 1866a; *C. inermis* Davaïne, 1877a; *C. tæniæ saginatæ* Leuckart, 1880; *C. “cellalosæ”* Ward, 1895; *Cysticercus bovis* (Cobbold, 1866) Schneidemuehl, 1896; *Cysticercus tæniæ saginatæ* (Leuckart) Schneidemuehl, 1896.

described as distinct species. One of these forms (*Tænia saginata abietina*) is of special interest to American physicians in so far that the only specimen ever taken was collected from an Indian in this country. It was first described as a variety of *Tænia solium*, but part of the original material has been reexamined, both by Leuckart and myself, and the characters found indicate that it is more closely related to *Tænia saginata*. Owing to the small amount and poor condition of the original material it is difficult to pass judgment upon the form; without further specimens, I should view it as a dwarfed specimen of *Tænia saginata*, but in order to direct special attention to it, in the hope that further specimens may be found, it is here accepted as a special form, leaving open the question as to whether it represents simply a variation, a variety, or a subspecies. One would scarcely be justified, at least at present, in giving it specific rank.

Weinland's Chippewa Tapeworm—*TÆNIA SAGINATA ABIETINA*^a (Weinland, 1858) Leuckart, 1886.

[Figs. 35 to 38.]

SUBSPECIFIC DIAGNOSIS.—*Tænia* (*Tæniarhynchus*) *saginata*: Length of strobila unknown; fragment measured "several feet in length." Head, neck, and mature segments unknown, but from resemblance of uterus to that of *T. saginata* the head

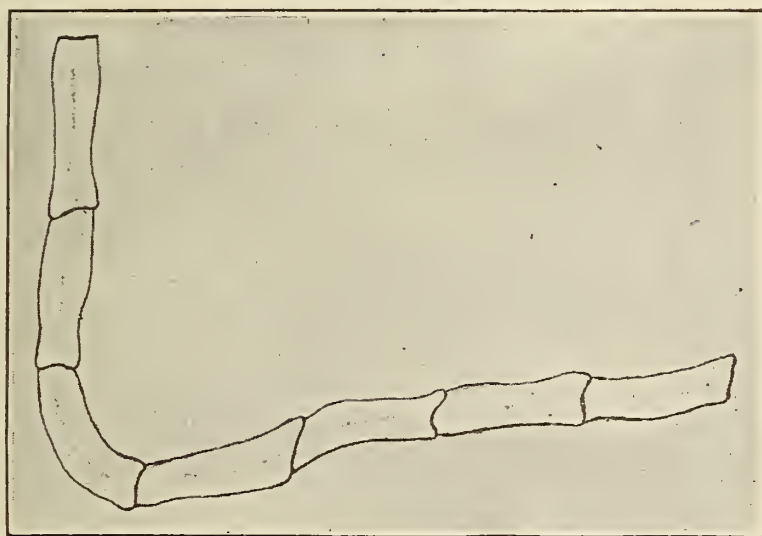


FIG. 35.—Strobila of *Tænia saginata abietina*. Natural size. (After Weinland, 1861, fig. 18.)

is assumed to be unarmed. Gravid segments very thin, nearly transparent, equally narrow, attain 12 mm. long by 4 mm. broad; calcareous corpuscles very numerous, round to oval, may attain $17.6\ \mu$; genital pore very small, about $\frac{5}{8}$ of length of segment from anterior margin; uterus with straight median stem and 30 to 40 lateral branches each side, generally straight, "never arborescently divided nor furcated at the ends, with the exception of the foremost and hindmost in each joint, which run, the former forward, the latter backward, both being forked and crooked." Eggs 31 to $37.5\ \mu$ by 30 to $33.9\ \mu$.

^a SYNONYMS.—*Tænia solium abietina* Weinland, 1858; *T. abietina* Weinland, 1858, of Davaine, 1873a; *Tenia abietina* (Weinland, 1858) Guzzardi Asmundo, 1885a; *Tænia saginata abietina* (Weinland, 1858) Leuckart (Hoyle), 1886.

HABITAT.—Intestine of man at Sault Ste. Marie, Lake Superior. Type, no. 9713 U. S. P. H. & M. H. S.

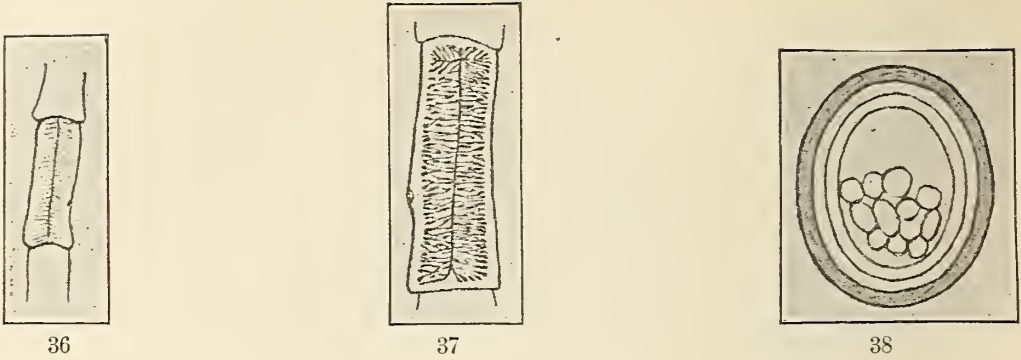


FIG. 36.—Segment of same showing the uterus. Natural size. (After Weinland, 1861, fig. 19.)

FIG. 37.—Gravid segment. $\times 2$. (After Leuckart, 1863, 289, fig. 80.)

FIG. 38.—Egg of same. Greatly enlarged. (After Weinland, 1861, fig. 20.)

The African Tapeworm—*TÆNIA AFRICANA* Linstow, 1900.

[Figs. 39 to 51.]

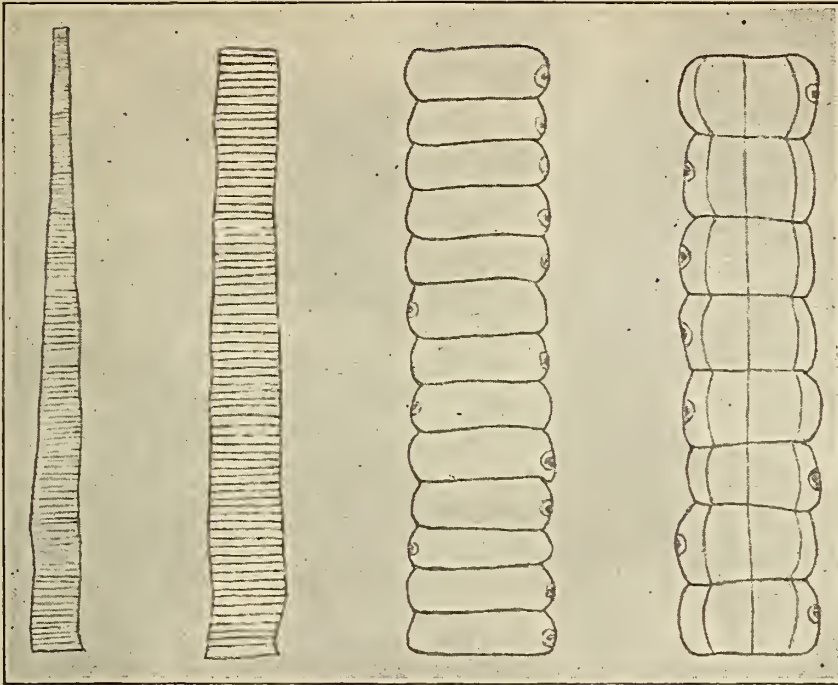
SPECIFIC DIAGNOSIS.—*Tænia* (*Tæmarhynchus*) (p. 26): Strobila attains 1.4 meters in length and is composed of about 600 segments. Scolex unarmed, very small, 1.38 mm. broad, 1.03 mm. thick, 0.47 mm. long. Suckers circular, 0.63 mm., lumen $88\ \mu$; “apical sucker” 0.16 mm. Segments all broader than long, as follows: Immediately back of head, 0.16 mm. long by 1.78 mm. broad by 0.59 mm. thick; anterior segments, 1 by 5 by 0.75; 2 by 7 by 1.06; in middle of worm, 3 by 9 by 1.20; terminal segments, 7 by 12 to 15 by 1.35. Segments, about 150th segment from head and 2 mm. long, are mature; segments 7 mm. long are gravid. Cortical layers to middle layer in the proportion of 11:8:11. Ventral canals 0.43 to 0.82 mm. in diameter, their center bearing the relation of 14:72:14 to the transverse diameter of the segment; transverse canals with diameter $\frac{1}{3}$ as great as the dorso-ventral diameter of the segment. Three longitudinal nerves, close to and lateral of ventral canals, the center nerve crescentic on cross-section, 0.14 mm. broad, the smaller nerves $70\ \mu$ broad. Calcareous corpuscles oval, concentric, 10.4 by $16.9\ \mu$, lacking in anterior and mature segments, but present in gravid segments, and numerous in terminal proglottids. Genital pores irregularly alternate in equator of segment; genital sinus funnel shaped. Male organs: Testicles numerous, scattered throughout middle layer, 88 to $114\ \mu$, or 70 to $53\ \mu$; vas deferens very convoluted, extending $\frac{2}{7}$ ths across the segment; thickly setose cirrus $52\ \mu$ broad, makes a loop in the cirrus pouch; cirrus pouch pyriform, with thick wall. Female organs: Ovary composed of two fan-shaped wings, composed of club-shaped tubes centering toward the shell-gland, occupies the 2nd and 3rd transverse fourths of the segment, and leaves but a narrow proximal and distal margin of the segment free; vitellogene gland distal, 1.70 mm. broad by $79\ \mu$ long; shell-gland median, globular, 0.21 to 0.23 mm.; vagina setose, $35\ \mu$ broad, runs almost straight from vulva to the shell-gland, near which it widens into a 0.17 by 0.07 mm. receptaculum seminis; on each side of median uterine stem, 15 to 24 lateral unbranched pouches, which are longer than median stem and spread out like a fan. Embryophore 31 to 39 by $33.8\ \mu$, with thick radially-striated shell; hooks of onchosphere, $7.8\ \mu$ long.

Cysticercus: Unknown.

HABITAT.—Adult in intestine of man. Suspicion has fallen on the zebu as possibly being the intermediate host.

GEOGRAPHIC DISTRIBUTION.—Known only for Langenburg, German East Africa.

MEDICAL SIGNIFICANCE.—Unknown.



FIGS. 39 to 42.—Four portions of strobila of *Tania africana*. (After Linstow, 1900, 487, figs. 1-4.)

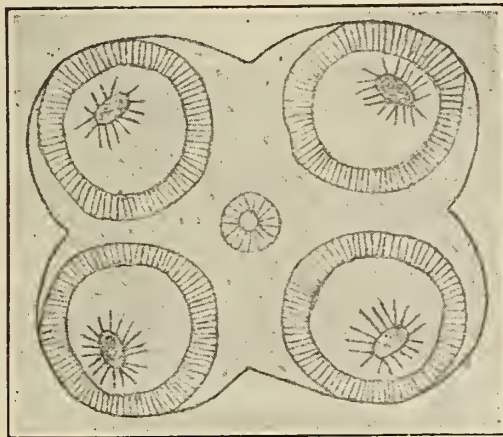


FIG. 43.—Apex view of head of same. Greatly enlarged. (After Linstow, 1900, 487, fig. 5.)

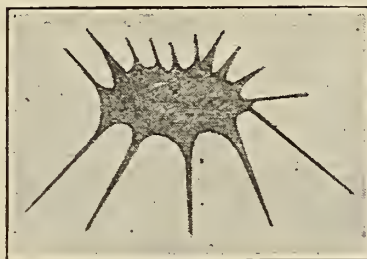


FIG. 44.—Lumen of sucker. Greatly enlarged. (After Linstow, 1900, 487, fig. 6.)

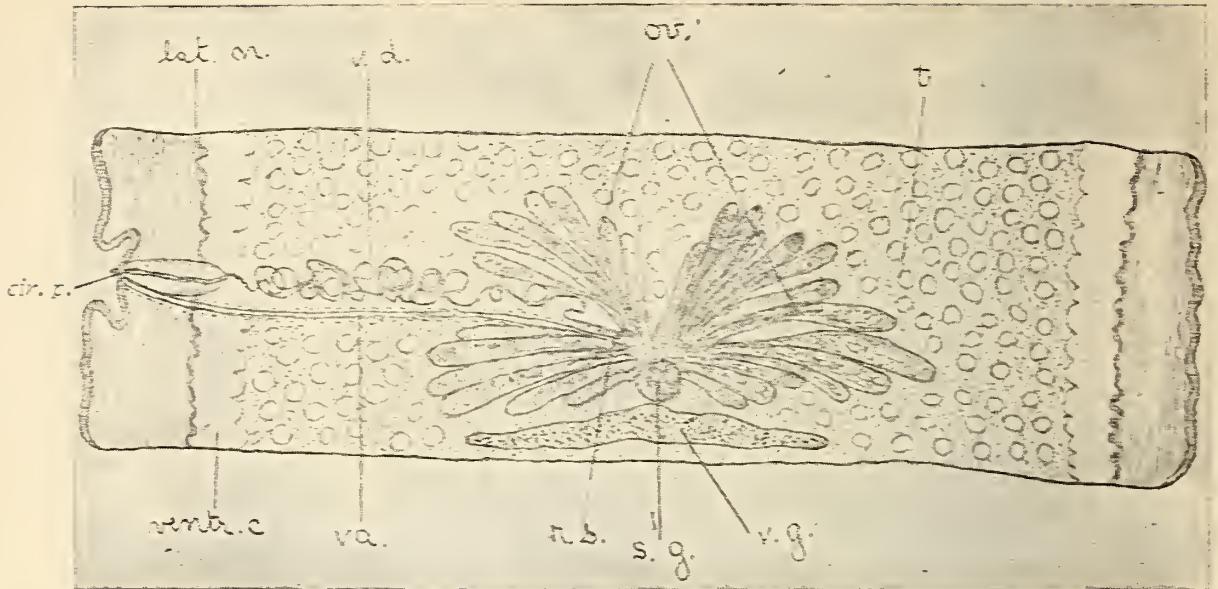


FIG. 45.—Diagram of frontal section of mature segment of same, to show the anatomy: *cir. p.*, cirrus pouch; *lat. n.*, lateral nerve; *ov.*, ovary; *r. s.*, receptaculum seminis; *s. g.*, shell gland; *t.*, testicles; *va.*, vagina; *ventr. c.*, ventral canal; *v. d.*, vas deferens; *v. g.*, vitellogene gland. Enlarged. (After Linstow, 1900, 488, fig. 7.)

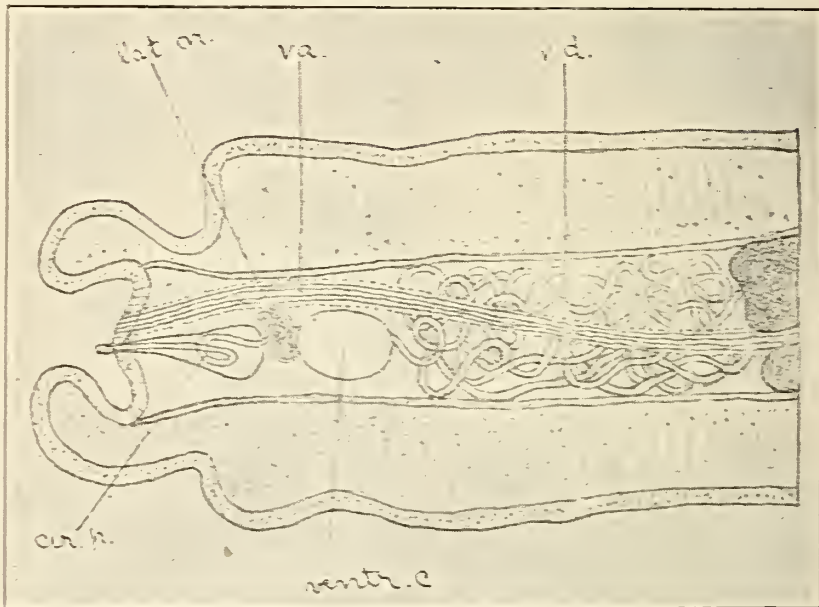


FIG. 46.—Transverse section of marginal portion of segment; same lettering as in fig. 45. (After Linstow, 1900, 488, fig. 8.)

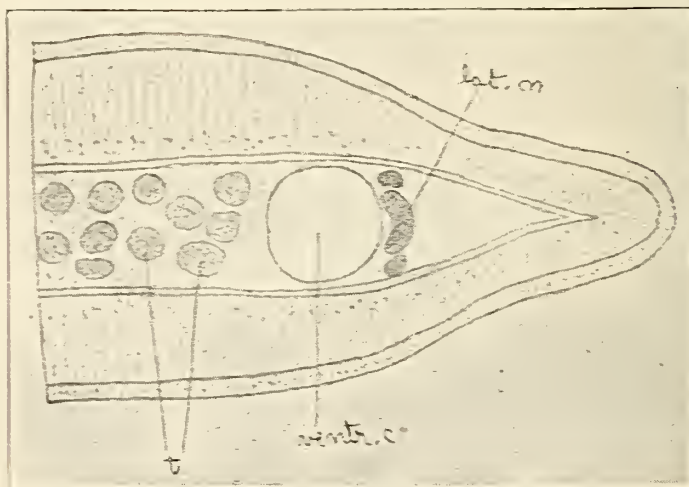
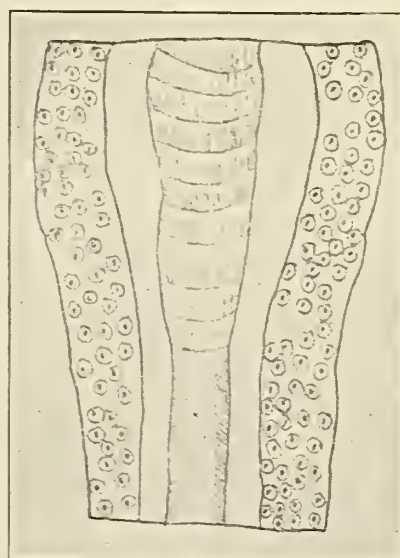
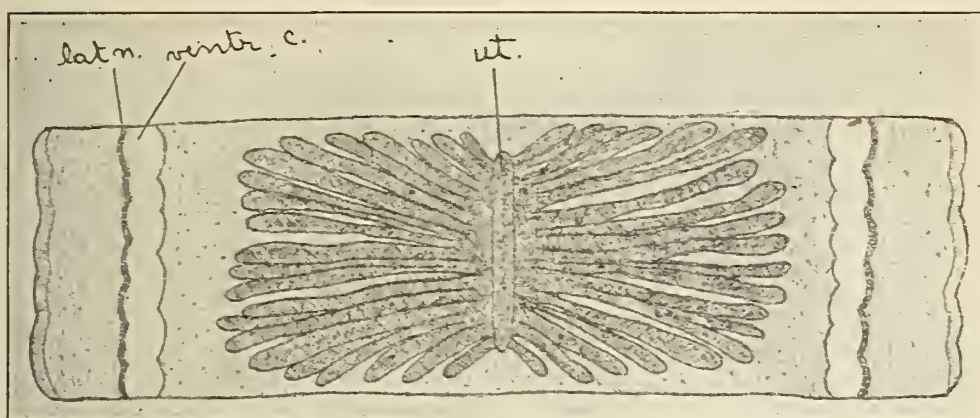
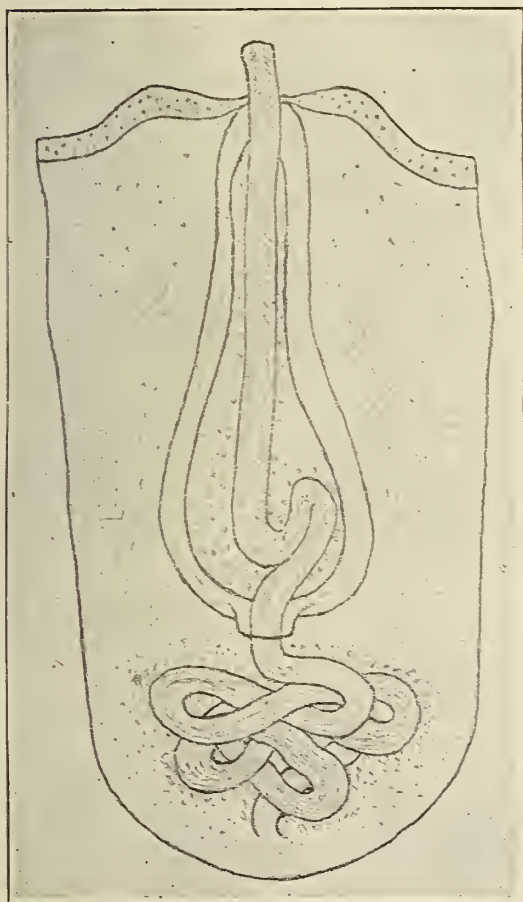


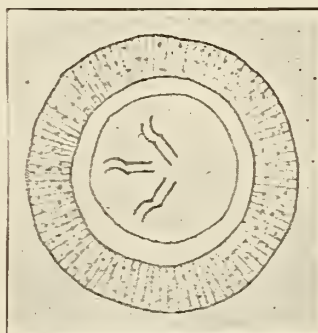
FIG. 47.—Transverse section of marginal portion of segment at another point; same lettering as in fig. 45. (After Linstow, 1900, 488, fig. 9.)



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FIG. 48.—Frontal section of a gravid segment: *lat. n.*, lateral nerve: *ut.*, uterus: *ventr. c.*, ventral canal. (After Linstow, 1900, 489, fig. 10.)

FIG. 49.—Vagina, close to genital sinus, and showing the setæ. (After Linstow, 1900, 489, fig. 11.)

FIG. 50.—Cirrus pouch, cirrus, and portion of the vas deferens. (After Linstow, 1900, 489, fig. 12.)

FIG. 51.—Egg of *Tænia africana*. Greatly enlarged. (After Linstow, 1900, 489, fig. 13.)

TÆNIA HOMINIS^a Linstow, 1902.

[Figs. 52 to 53.]

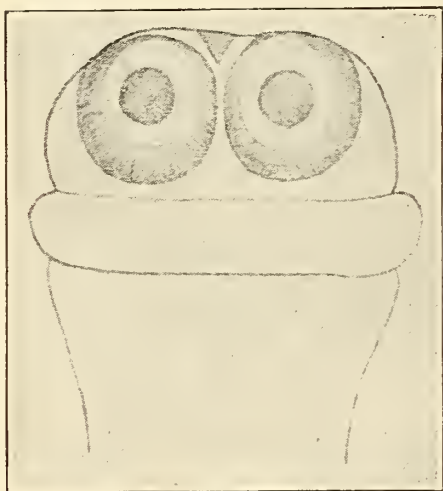
SPECIFIC DIAGNOSIS.—*Tænia* (*Tæniarhynchus*) (p. 26): Strobila 70 mm. long; back of scolex it is 1.11 mm. broad, posteriorly 1.97 mm. Scolex 2.01 mm. broad by 1.34 mm. long. Rostellum unarmed, rudimentary, $240\ \mu$ broad, $75\ \mu$ long. Suckers with lumina (0.60 mm. deep) running postero-anteriorly, so that they are circular on cross section. Genital organs not developed in specimen examined. Back of suckers a circular ridge. Possibly strobila grows as large as *T. saginata*. Dorsal and ventral cortical layer as broad as inner layer. Calcareous corpuscles very numerous, arranged in concentric layers. No black pigment present in type specimen. Ventral canals $16\ \mu$ lateral of dorsal canals; the ventral canals run in the 2d and 5th sixths of lateral diameter, and are connected with transverse canals at distal border of each segment; dorsal canals surrounded by radially running muscles. Longitudinal nerve closely lateral of ventral canals.

Cysticercus: Unknown.

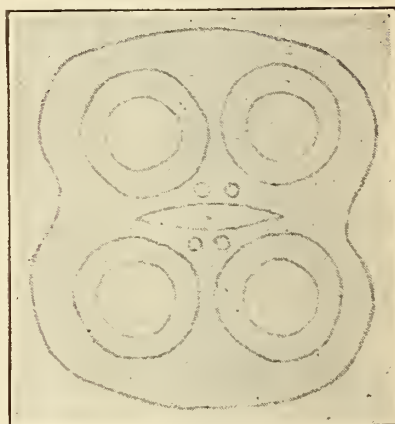
HABITAT.—Adult in intestine of man.

GEOGRAPHIC DISTRIBUTION.—Known only for Aschabad, Asiatic Russia.

MEDICAL SIGNIFICANCE.—Unknown.



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FIG. 52.—Head of *Tænia hominis*; note the circular ridge back of the suckers. Greatly enlarged. (After Linstow, 1902, 770, fig. 3.)

FIG. 53.—Transverse section of same, through the suckers. (After Linstow, 1902, 770, fig. 4.)

Subgenus TÆNIA.^b

SUBGENERIC DIAGNOSIS.—*Tænia* (p. 24): Rostellum distinct, and armed with a double crown of hooks of two sizes; segments usually numerous, may be over 500

^aSYCNYM.—*Tænia hominis* Linstow, 1902 (not *T. armata hominis* Brera, 1808a; not *Tænia lata hominis* Bloch, 1782a; not *Tænia albopunctata hominis* Diesing, 1850a; not *Tænia mediocanellata hominis* Kuechenmeister, 1852f).

^bSYNONYMS.—*Tænia* Linnaeus, 1758a; *Tænia* Scopoli, 1777; *Hydatigena* Gœze, 1782a; *Megocephalos* Gœze, 1782a; ? *Pseudoechinorhynchus* Gœze, 1782a; *Finna* Werner, 1786, and Brera, 1809a; *Vesicaria* Mueller, 1787, and Schrank, 1788; *Hydatula* Abildgaard, 1790a; ? *Hæruca* Gmelin, 1790a; *Hydatis* Blumenbach, 1797; *Cysticercus* Zeder, 1800a; *Alyscminthus* Zeder, 1800a; *Halysis* Zeder, 1803a; *Cisticercus* Rudolphi, 1805; *Physchiosoma* Brera, 1809a; *Finna* Brera, 1809a; *Gæziana* Rudolphi, 1810a; *Hydatigera* Lamarck, 1816; *Fischiosoma* delle Chiaje, 1825a for *Physchiosoma*; *Trachelocampylus* Fredault, 1847b; *Arhynchotænia* Diesing, 1850a; *Halysis* Goldberg, 1855a; *Acanthotrias* Weinland, 1858; *Cystotænia* Leuckart, 1863; *Neotenia* Soderro, 1886; *Neotænia* Braun, 1894a; *Cysticerkus* and *Cystizerkus* of several authors

present; vitellogene gland triangular, one side parallel to posterior margin of the segment. Larva a cysticercus which lives in mammals; adults in intestine of meat-eating mammals.

TYPE SPECIES.—*Tænia solium* Linnæus, 1758.

The Pork Tapeworm—*TÆNIA SOLIUM* ^a Linnæus, 1758.

[Figs. 54 to 61.]

SPECIFIC DIAGNOSIS.—*Tænia* (*Tænia*) (p. 36): Strobila attains 2 to 3.5 meters or more in length, greatest breadth 7 to 8 mm.; composed of about 800 to 900 segments. Head globular, 0.6 to 1 mm. in diameter; rostellum short but prominent; hooks 22 to 32 in number, alternating large (160 to 180 μ) and small (110 to 140 μ); suckers 0.4 to 0.5 mm. in diameter. Unsegmented neck present. Genital pores irregularly alternating, slightly back of equator of segment. Sexually mature proglottids measure 2.5 to 3 mm. long by 4.5 to 5 mm. broad; vagina with setæ; part of smaller ovarian lobe (on pore side of segment) cut off by vagina, lobes transversely oval; testicles 0.12 to 0.15 mm.; seminal vesicle absent; length of cirrus pouch? Gravid (end) proglottids attain 10 to 12 mm. long by 5 mm. wide; uterus with 7 to 14 thick, lateral, dichotomous branches each side. Calcareous corpuscles sparse, attain 0.012 mm. Eggs oval or almost round, shell thin and usually destroyed; embryophore thick, yellowish to dark brown, 31 to 36 μ .

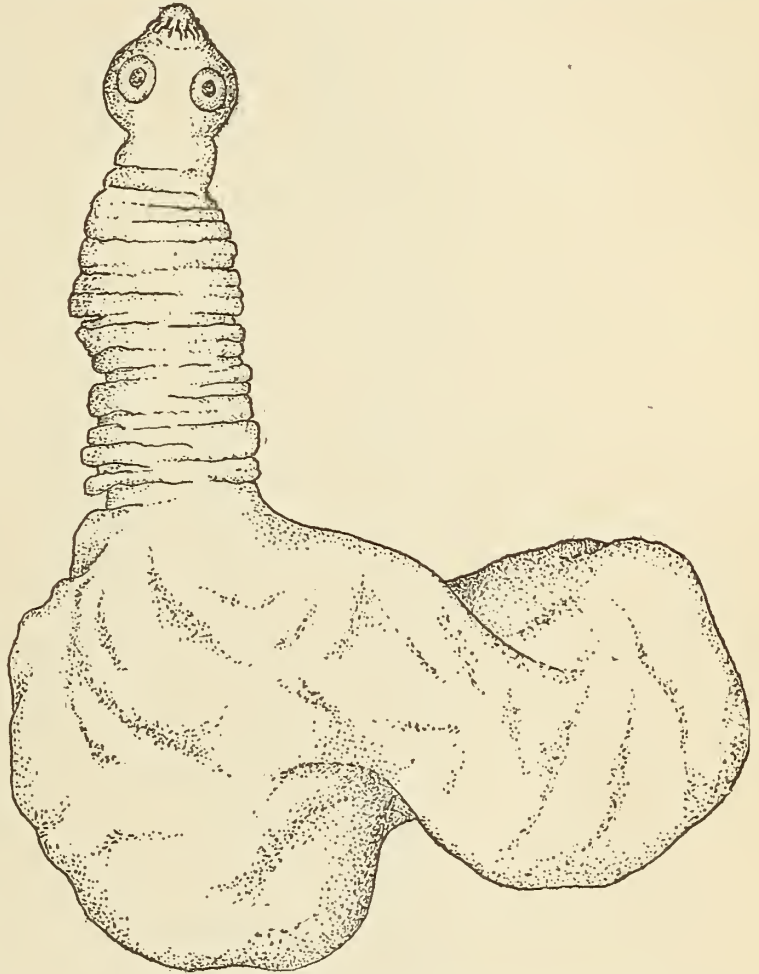


FIG. 54.—An isolated Pork-measle Bladder Worm (*Cysticercus cellulosæ*), with extended head. Greatly enlarged. (After Stiles, 1898a, 90, fig. 76.)

Cysticercus: *C. cellulosæ*,^b ellipsoid, 6 to 10 mm. long by 5 to 10 mm. broad, with a white spot corresponding to the invaginated head; head as in adult; the bladder contains but little fluid.

HABITAT.—Adult in small intestine of man; experiments to bring about intestinal infections in swine, dogs, guinea pigs, rabbits, and apes (*Macacus cynomolgus*) have been negative. Cysticercal stage in muscles of wild boar (*Sus scrofa*) and swine (*S. scrofa domestica*); occasionally in man (*Homo sapiens*); also reported for moustached monkey (*Cercopithecus cephus*), patas guenon (*C. patas*), barbary macaque

^aSYNONYMS.—*Tænia solium* Linnæus, 1758a, s. str., after elimination of *T. saginata* and *T. hydatigena*; *T. cucurbitina* Pallas, 1766, and Bloch, 1782a; *T. cucurbitina pellucida* Goeze, 1782a; *T. cucurbitina, plana, pellucida* Goeze, 1782a; ? *T. vulgaris* Werner, 1782 (not Linnæus, 1758), renamed *T. dentata* Batsch, 1786a (not Nicolai, 1830); *T. solitaria* Leske, 1784 or 1785 (not accessible, see Seeger, 1852); *T. plana pellucida* Goeze, 1782 of Gmelin, 1790a; *Tænia armata humana* Brera, 1802a; *Halysis solium* (Linnæus, 1758) Zeder, 1803a; *Tænia armata hominis* Brera, 1808a; *T. humana armata*

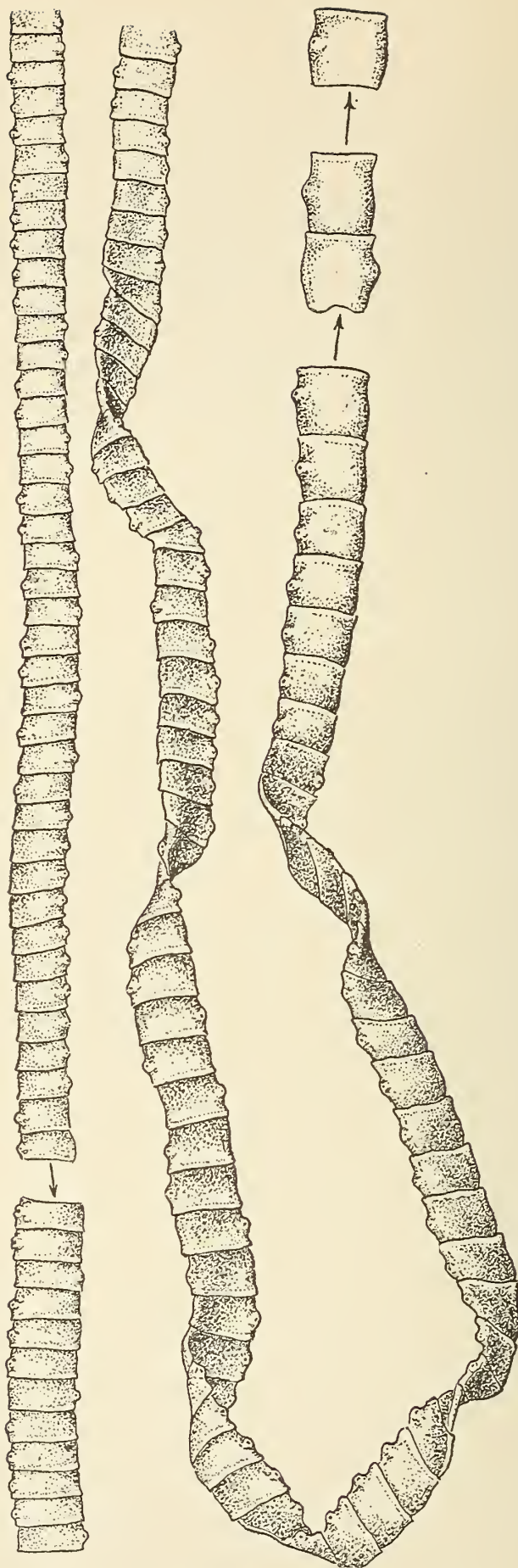


FIG. 55.—Several portions of an adult Pork-measle Tapeworm (*Tenia solium*). Natural size. (After Stiles, 1898a, 91, fig. 77.)

Rudolphi, 1810a; ? *T. fenestrata* delle Chiaje, 1833a; *T. solium* Linnæus, 1758, partim, Kuechenmeister, 1852f; *T. hamoloculata* Kuechenmeister, 1855a; *T. turbinata* Kœberlé, 1861a; *T. melanocephala* Kœberlé, 1861a; *Tenia solium* (Linnæus, 1758) Beneden,

(*Macacus inuus*), brown bear (*Ursus arctos*), dog (*Canis familiaris*), cat (*Felis catus domestica*), black rat (*Mus rattus*), sheep (*Ovis aries*), and roe deer (*Capreolus caprea*).

GEOGRAPHIC DISTRIBUTION.—Practically cosmopolitan, following the hog.

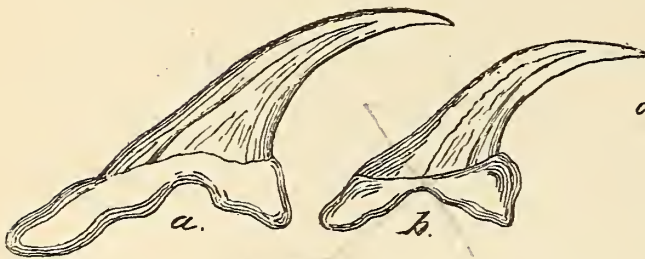
SPECIAL MEDICAL SIGNIFICANCE.—This is the most dangerous adult tapeworm of man, because of the danger of auto-reinfection leading to cysticercosis (see p. 68): hence treatment should be instituted without unnecessary delay.

PREVENTION.—Eat pork only when it is well cooked or well cured. A person with this tapeworm should never defecate in a place to which hogs have access. Box privies should never be placed near pigpens.

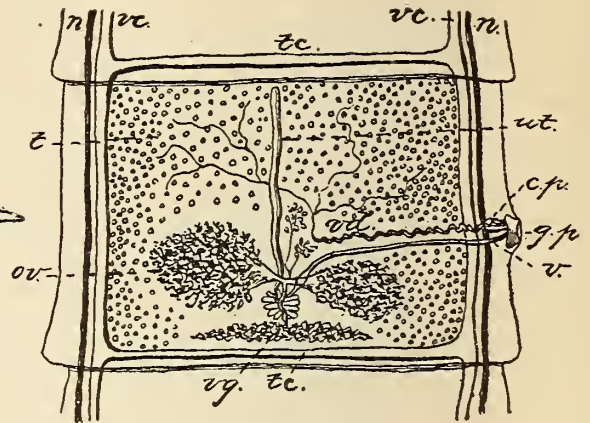
1861a; *T. cucurbitina* Goeze of Beneden, 1861a; *Tenia* [(*Cystotania*)] *solum* Linnæus of Leuckart, 1863; *T. (Cysticercus) acanthotriax* (Weinland, 1858) Leuckart, 1863; *T. tenella* Cobbold, 1874v (not Pallas, 1781); *T. solium fœnestrata* Colin, 1876a, and Maggiora, 1891; *T. solium minor* Guzzardi Asmundo, 1885a; *Tenia tenella* (Cobbold, 1874) Guzzardi Asmundo, 1885a; *Tenia scalariforme* Notta, 1885; *T. solium scalariforme* Notta, 1885; *T. officinalis* Bos, 1894a; *T. tenella* Pepper, 1894.

BIBLIOGRAPHY.—For zoological discussion see Leuckart, 1880, 617–713, figs. 274–303; for medical literature see Stiles & Hassall, Index-Catalogue of Medical and Veterinary Zoology.

^b SYNONYMS.—*Vesicaria lobata* Fabricius, 1783; *Finna* Werner, 1786; *Finna humana* Fischer in Werner & Fischer, 1786; *Tenia hydatigena* Fischer, 1788b and 1789a (not Pallas, 1766); *Hydatis piriformis* Fischer, 1789a; *Tenia cellulosa* Gmelin, 1790a; *T. finna* Gmelin, 1790a; *Vesicaria hygroma humana* Schrank, 1793 (not accessible); *V. finna suilla* Schrank, 1793 (not accessible); *Tenia albopunctata* Treutler, 1793; *T. pyriformis* Treutler, 1793; *Hydatis finna* (Gmelin, 1790a) Blumenbach, 1797 (not accessible) and 1816a; *H. cellulosa* (Gmelin, 1790a) Virey, 1798; *H. humana* Blumenbach, –?– (not accessible); *Tenia muscularis* Jærdens, 1802a; *T. pyriformis* Jærdens, 1802a; *T. hydatigena anomala* Steinbuch, 1802 (not accessible); *T. collulosa* Treutler of Zeder, 1803a; *Cysticercus albopunctatus* (Treutler, 1793) Zeder, 1803a; *C. pyriformis* (Treutler, 1793) Zeder, 1803a; *C. finna* (Gmelin, 1790) Zeder, 1803a; *Cysticercus finnus* (Gmelin, 1790) Lænnec, 1804 and 1812; *C. dicystus* Lænnec, 1804 and 1812; *C. fischerianus* Lænnec, 1804 and 1812; *Cisticercus finna* (Gmelin, 1790a) Rudolphi, 1805; *Cysticercus cellulosa* (Gmelin, 1790a) Rudolphi, 1808a; *Fischiosoma pyriforme* (Treutler, 1793) Brera, 1809a; *Physchiosoma pyriforme* (Treutler, 1793) Brera, 1809a; *Finna cisticercus* Zeder of Brera, 1809a; *Finna muscularis* (Jærdens, 1802) Brera, 1809a; ?*Cysticercus canis* Rudolphi, 1810a and Kœberlé, 1861a; *Tenia cellulosa* (Gmelin, 1790) Lænnec, 1812; *C. cellulosa* Lamarck, 1816; *Hydatigera cellulosa* Lamarck, 1816; *Tenia hydatigena suilla* Fischer of delle Chiaje, 1825a; *Cysticercus cellulosa* (Gmelin, 1790) Cuvier, 1825a; *Finna cysticercus* Zeder of delle Chiaje, 1825a; *Vesicaria finna* Schrank (not accessible) of delle Chiaje, 1825a; *V. hygrometra* Schrank (not accessible), of delle Chiaje, 1825a; *Hydatis lanceolata* Lam. (not accessible) of delle Chiaje, 1825a; *Tenia albopunctata* Tschudi, 1837; ?*T. hydatigena* MS. in Creplin, 1840a; *Trachelocampylus* Fredault, 1847b; *Tenia albopunctata hominis* Treutler, of Diesing, 1850a; *Vesicaria lobata suilla* Brera, of Diesing, 1850a; *Vermis vesicularis* Brera, of Diesing, 1850a; *Cysticercus cellulosa* (Gmelin, 1790) Diesing, 1850a; ?*C. vesicæ hominis* Creplin, 1840, of Diesing, 1850a; *Hydatigena cellulosa* Gmelin of Diesing, 1850a; *Acanthotriax* Weinland, 1858; *Cysticercus acanthotriax* Weinland, 1858; ?*C. vesicæ* Creplin, 1840, of Moquin-Tandon, 1860; *Tenia hydatigena eremita* Werner of Kœberlé, 1861a; *T. hydatigena* Kœberlé, 1861a; *Cysticercus solium* (Linnæus, 1758) Kœberlé, 1861a; *C. turbinatus* Kœberlé, 1861a; *C. melanocephalus* Kœberlé, 1861a; *C. multilocularis* Kuechenmeister, –?–; *C. suis* Cobbold, 1869; *C. racemosus* Heller, 1874a; *C. botryoides* Heller, 1874a; *Neotenia Sodero*, 1886; *Neotania* Braun, 1894a; *Cysticercus cellulosi* Ward, 1895; *Cysticercus cellulosa* (Gmelin, 1790a) Schneidemuehl, 1896; *Tenia hydatigera* Fischer of Stiles, 1898.



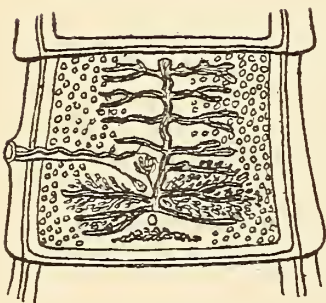
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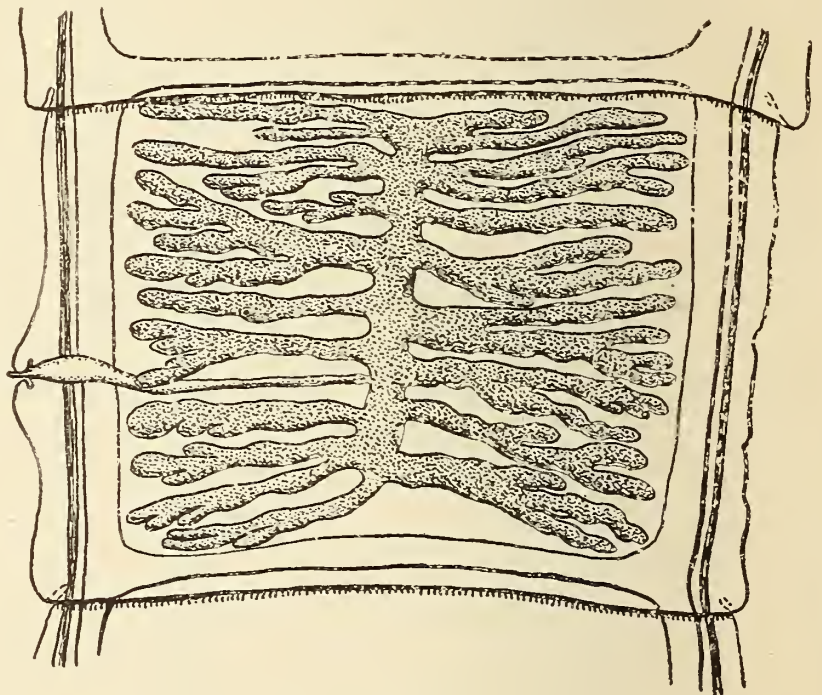
57

FIG. 56.—Large (a) and small (b) hooks of the Pork-measle Tapeworm (*Taenia solium*). $\times 280$. (After Leuckart, 1880, 661, fig. 293.)

FIG. 57.—Mature sexual segments of Pork-measle Tapeworm (*Taenia solium*), showing the divided ovary on the pore side: c. p., cirrus pouch; g. p., genital pore; n., nerve; ov., ovary; t., testicles; t. c., transverse canal; ut., uterus; va., vagina; v. c., ventral canal; v. d., vas deferens; v. g., vitellogene gland. $\times 10$. (After Leuckart, 1880, 665, fig. 294.)



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FIG. 58.—Segment of Pork-measle Tapeworm (*Taenia solium*) in which the uterus is about half developed. $\times 2$. (After Leuckart, 1880, 666, fig. 295.)

FIG. 59.—Gravid segment of Pork-measle Tapeworm (*Taenia solium*), showing the lateral branches of the uterus, enlarged. (After Stiles, 1898a, 94, fig. 81.)

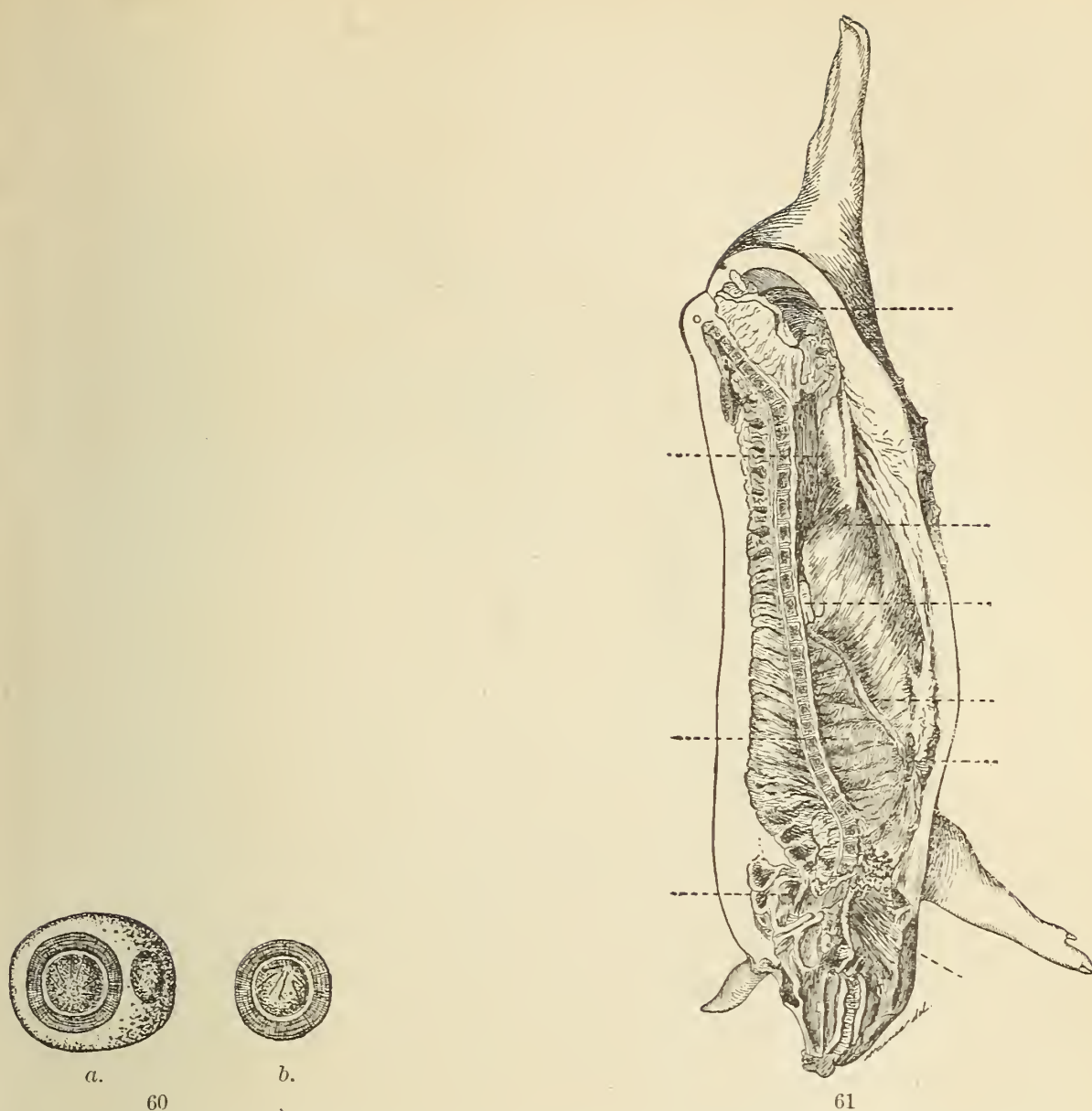


FIG. 60.—Eggs of Pork-measle Tapeworm (*Tania solium*): *a*, with primitive vitelline membrane; *b*, without primitive vitelline membrane, but with striated embryophore. $\times 450$. (After Leuckart, 1880, 667, fig. 297.)

FIG. 61.—Half of hog, showing the portions most likely to become infested with Pork-measles. (After Ostertag, 1895, 387, fig. 79.)

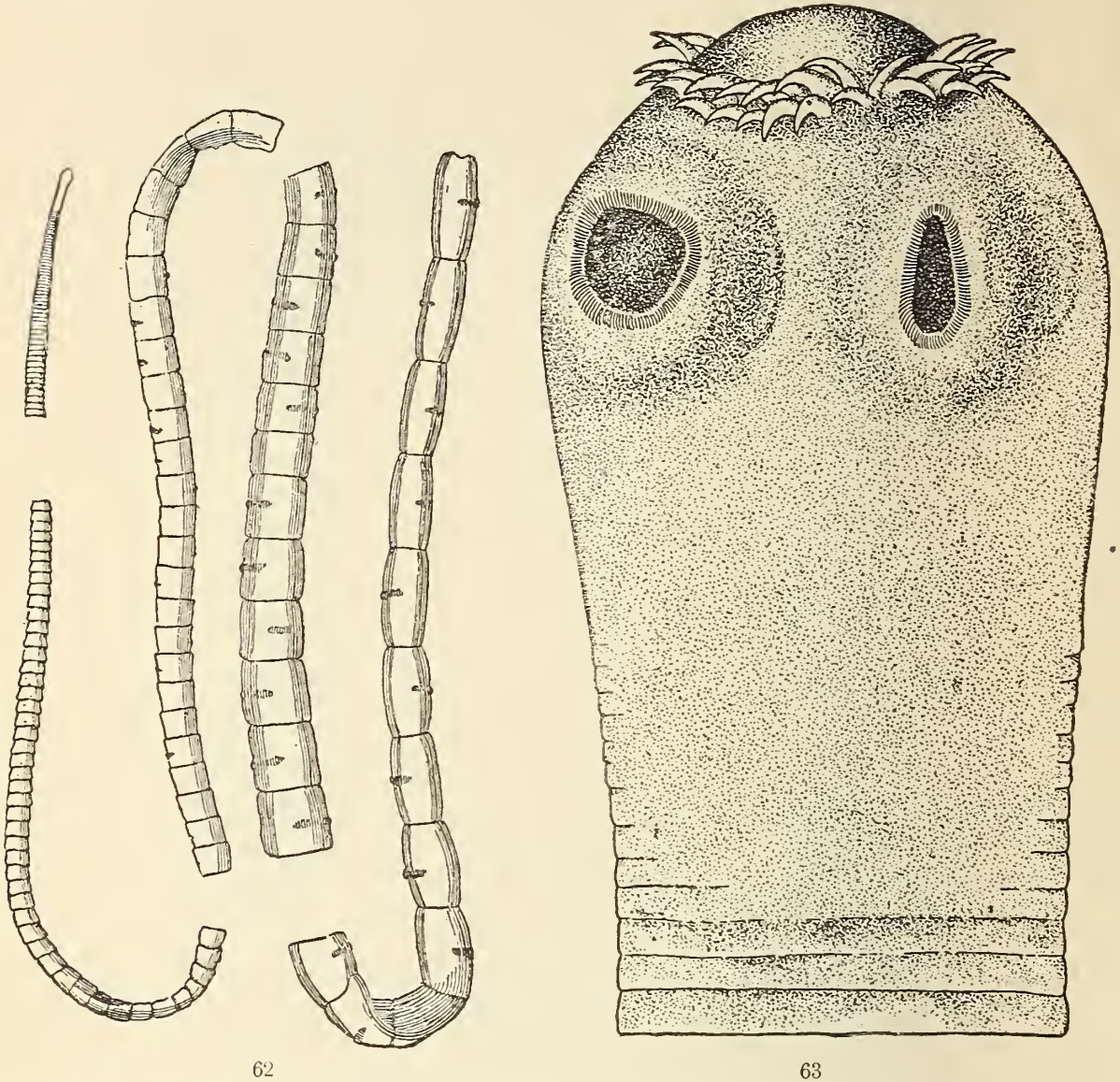
The Pisiform Tapeworm—*TÆNIA PISIFORMIS*^a (Bloch, 1780) Gmelin, 1790.

[Figs. 62 to 65.]

SPECIFIC DIAGNOSIS.—*Tænia* (*Tænia*) (p. 36): Strobila attains 0.5 to 2.0 meters in length. Head, 1.5 to 2 mm. in diameter; rostellum powerful, armed with a double row of 34 to 48 hooks, alternating large (225 to 294μ) and small (132 to 177μ); ventral root of small hooks bifid. Neck, 1 to 2 mm. long, slightly narrower than head. Genital pores irregularly alternate, very prominent, giving the porose border of the segment a convexity. Segments at first narrow and much shorter than broad, becoming square about 25 cm. from the head; the straight posterior border is broader than the anterior, and thus gives the margin of the worm a serrate appearance;

^a **SYNONYMS.**—? *Tænia canina solium* Werner, 1782; ? *T. cucurbitina* γ [*canis*] Batsch, 1786a; ? *T. cucurbitina* Gmelin, 1790a; ? *T. serrata canis domestici et vulpis* Rudolphi, 1793a; *Tenia serrata* Gœze of Beneden, 1861a; *Tænia serrata* of most authors since Kuechenmeister.

ovaries 2, in distal half of segment. Gravid segments, 30 to 40 in number, and representing about two-fifths of the length of the worm, 4 to 6 mm. broad by 10 to 17 mm. long; uterus with 8 to 10 irregularly branched lateral pouches. Embryophores ovoid, 36 to 40 by 31 to 36 μ .



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FIG. 62.—Strobila of *Tania pisiformis*. Natural size. (After Railliet, 1893a, 222, fig. 121.)

FIG. 63.—Head of *Tania pisiformis*, showing hooks, suckers, and anterior segments. $\times 40$. (After Stevenson, 1904, pl. 6, fig. 47.)

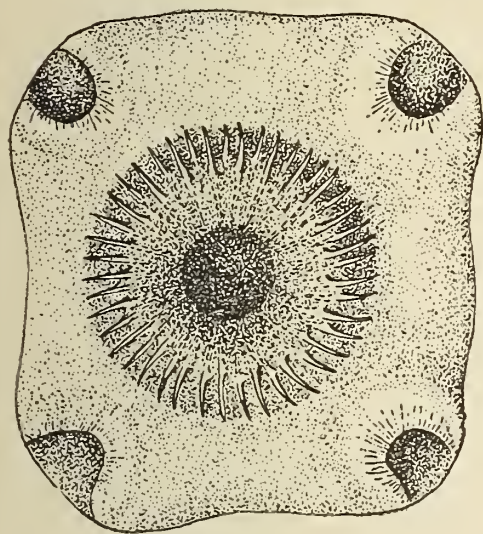
Cysticercus: *C. pisiformis*^a first develops to about 1 cm. or more in length in the liver of rabbits, etc., then wanders to the abdominal cavity, where it becomes encysted and increases in size, becoming pisiform to elongate.

^aSYNONYMS.—*Vermis vesicularis pisiformis* Bloch, 1780a; *Hydatigena pisiformis* (Bloch, 1780) Goeze, 1782a; *H. utriculenta* Goeze, 1782a; *H. cordata* Batsch, 1786a; *H. utricularis* Batsch, 1786a; *Vesicaris pisiformis* (Bloch, 1780a) Schrank, 1788; *V. utriculenta* (Goeze, 1782a) Schrank, 1788; *Tania pisiformis* (Bloch, 1780a) Gmelin, 1790a; *T. utricularis* (Batsch, 1786a) Gmelin, 1790a; *T. cordata* (Batsch, 1786a) Gmelin, 1790a; ? *T. putorii* Gmelin, 1790a; *Hydatula pisiformis* (Bloch, 1782a) Frœlich, 1803a; *Cysticercus pisiformis* (Bloch, 1780a) Zeder, 1803a; ? *C. putorii* (Gmelin, 1790a) Zeder, 1803a; *C. utriculentus* (Goeze, 1782a) Lænnec, 1804; *C. lineatus pisiformis* (Bloch, 1780a) Lænnec, 1812; *Hydatis pisiformis* (Bloch, 1780a) Lamarck, 1816; *Monostoma leporis* Kuhn, 1830; ? *Cysticercus cordatus* Tschudi, 1837; *C. elongatus* Leuckart, 1842; *Monostomum leporis* (Kuhn, 1830) Diesing, 1850a; *Hydatigena hepatis nurini* Diesing, 1850a; *Cysticercus serratus (pisiformis)* Kœberlé, 1861a; *C. pysiformis* Diesing of Beneden, 1861a.

HABITAT.—Adult in intestine of dogs (*Canis familiaris*) and other canines. *Cysticercus* in peritoneal cavity of rabbits (*Lepus cuniculus*), hares (*L. timidus*, *L. variabilis*), mice (*Mus musculus*), etc.

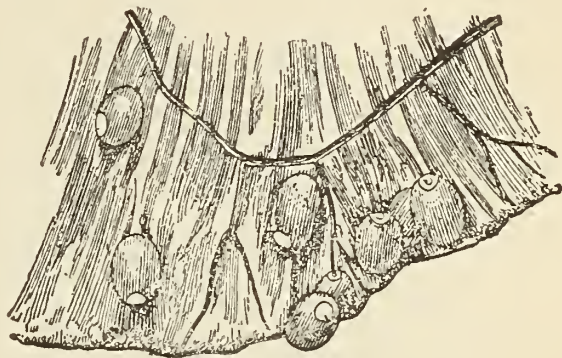
GEOGRAPHIC DISTRIBUTION.—Very extensive, probably more or less cosmopolitan.

MEDICAL SIGNIFICANCE.—Vital (1874) reports this tapeworm for man in one case in Algiers, but legitimate doubts arise regarding the correctness of his zoological determination.



64

FIG. 64.—Apex view of same. $\times 28$. (After Stevenson, 1904, pl. 6, fig. 49.)



65

FIG. 65.—Portion of mesentery of rabbit infected with *Cysticercus pisiformis*. Natural size. (After Railliet, 1893a, 216, fig. 114.)

The Thick Necked Cat-Tapeworm—*TÆNIA TENIÆFORMIS*^a (Bloch, 1780) Stiles & Stevenson, 1905.

[Figs. 66 to 67.]

SPECIFIC DIAGNOSIS.—Strobila attains 15 to 60 cm. in length. Head thick, cylindrical anteriorly, 1.7 mm. broad; rostellum short, armed with a double row of 26 to 52 hooks; alternating large (380 to 420 μ) and small (250 to 270 μ); suckers very prominent. Neck not distinct, as broad or broader than head. Anterior segments very short, the following cuniform, the terminal 8 to 10 mm. long by 5 to 6 mm. broad. Embryophore globular, 31 to 37 μ .

Cysticercus: *C. fasciolaris*,^b elongate, 3 to 20 mm. long, with small terminal caudal vesicle.

^a**SYNONYMS.**—*Tænia collo brevissimo* Bloch, 1782a; *T. serrata* Gœze, 1782a; ?*T. globulata* Gœze, 1782a; ?*T. moniliformis* Batsch, 1786a, not Pallas, 1781; *T. serrata felis* Gmelin, 1790a; *T. felis* Gmelin of Carlisle, 1794a; *Alyselminthus serratus* (Gœze, 1782a) Zeder, 1800a; *Halysis serrata* (Gœze, 1782a) Zeder, 1803a; *Tænia crassicolis* Rudolphi, 1810a; *T. serrata* a, *cati domest.* b, *sylvestr.* Schrank of Rudolphi, 1810a; *Halysi serrata* (Gœze, 1782a) Rudolphi, 1810a; *Halysis serrata* (Zeder) of Goldberg, 1855a; *Tænia crassicolis* Kœberlé, 1861a.

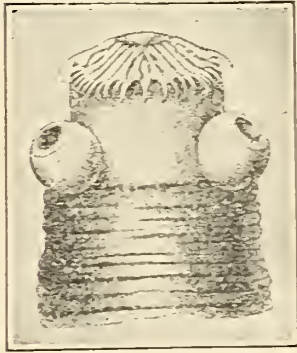
^b**SYNONYMS.**—*Vermis vesicularis muris* Hartmann, 1695b; *Fasciola muris hepaticæ* Røederer, 1762; *Tænia hydatigena* Pallas, 1766, in part; *T. hydatigena murini hepatis* Pallas, 1766; *Vermis vesicularis teniæformis* Bloch, 1760a; *Fasciola* sp. Merrem, 1781; *F. succata* Merrem of Gœze, 1782a; *Megocephalos* Gœze, 1782a, type; ? *Pseudoechinorhynchus* sp. Gœze, 1782a; *Tænia (Hydatigena) vesicularis fasciolata* Gœze, 1782a; *T. hydatigena* Werner, 1782; *T. vesicularis teniæformis* Bloch of Werner, 1782; *Vermis vesicularis teniæformis* Bloch of Batsch, 1786a; *Hydatigena teniæformis* Batsch, 1786a;

HABITAT.—Adult in small intestine of various felines, as the wild cat (*Felis catus*), domesticated cat (*F. catus domestica*), puma (*F. concolor*), etc.

Larva in liver of brown rat (*Mus decumanus*), black rat (*M. rattus*), house mouse (*M. musculus*), water vole (*Arvicola amphibius*), field vole (*A. arvalis*), long-eared bat (*Plecotus auritus*).

GEOGRAPHIC DISTRIBUTION.—Europe, Asia, North America; probably more or less cosmopolitan, following the rats.

MEDICAL SIGNIFICANCE.—Krabbe has suggested that this tapeworm may possibly occur as an occasional parasite in man, since chopped raw mice are eaten in Jütland as a folk remedy for retention of urine. I know of no case actually reported for man.



66



67

FIG. 66.—Head of *Tænia teniaeformis*. $\times 15$. (After Neumann, in Railliet, 1893a, 250, fig. 142.)

FIG. 67.—Larval stage of *Tænia teniaeformis*. Natural size. (After Leuckart, 1880, 450, fig. 202.)

Subgenus uncertain.

Ward's Nebraskan Tapeworm—*TÆNIA CONFUSA* a Ward, 1896.

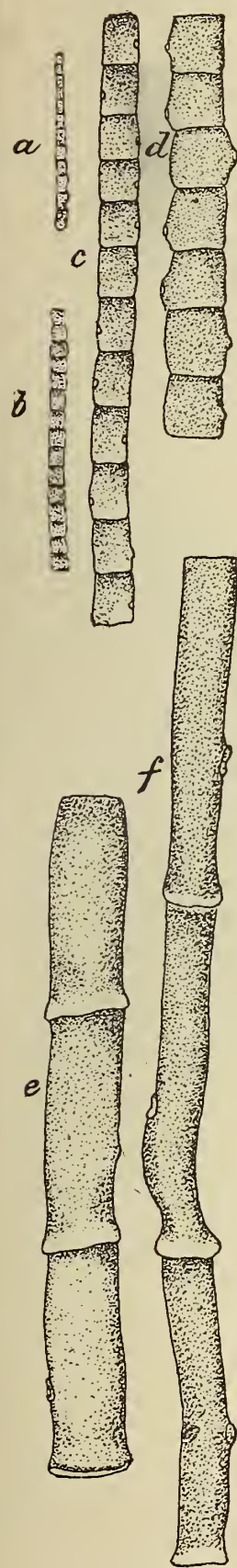
[Figs. 68 to 73.]

SPECIFIC DIAGNOSIS.—*Tænia* (subgenus uncertain) (p. 24): Strobila attains 5 to 8 mm. in length, greatest breadth 8 to 10 mm.; composed of about 750 to 800 segments. Head unknown. Neck segmented. Genital pore back of middle of lateral

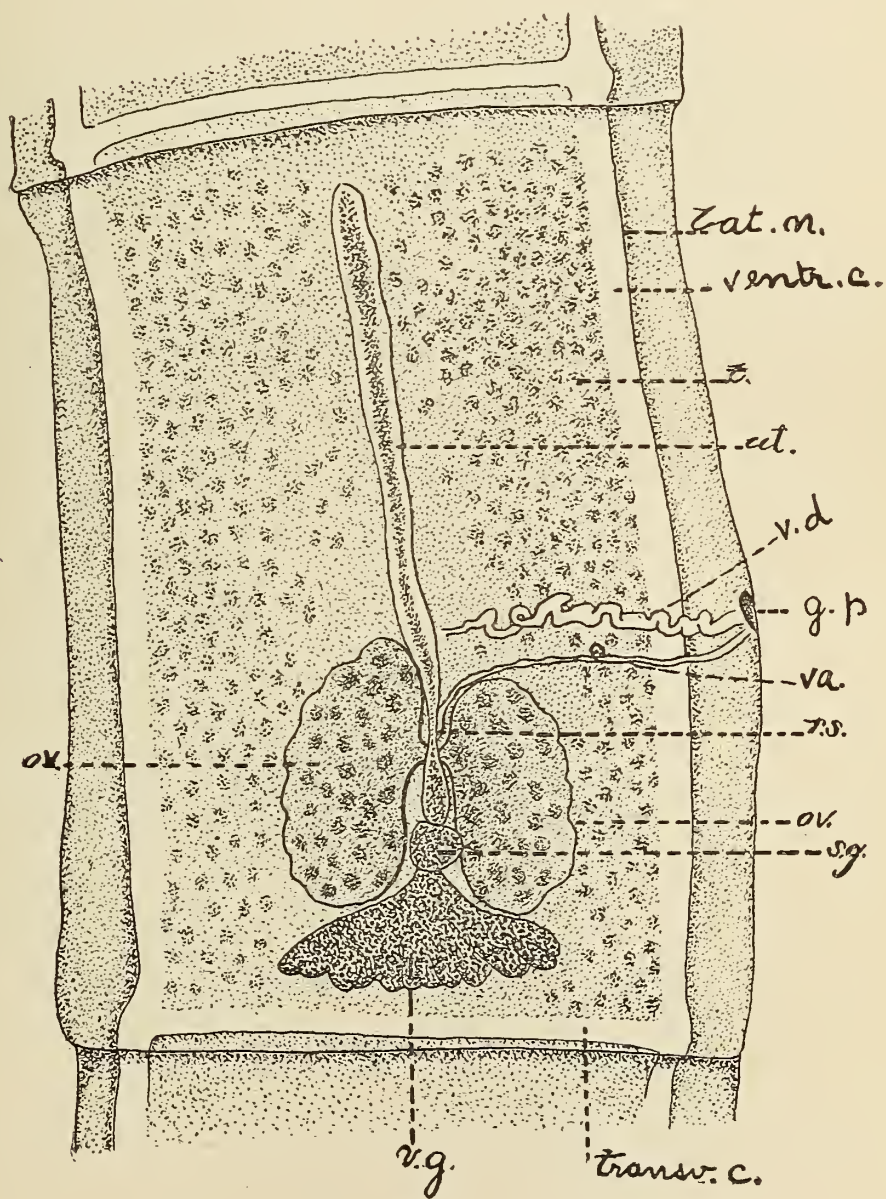
? *Echinorhynchus muris* Schrank, 1788; *Vesicaria tæniæformis*. (Batsch, 1786a) Schrank, 1788; ? *Hæruca muris* (Schrank, 1788) Gmelin, 1790a; *Tænia murina* Gmelin, 1790a, not Dujardin, 1845a; *T. hydatigena* Gmelin, 1790a; *T. vespertilionis* Gmelin, 1790a; *Vesicaria muris* Schrank, 1793; *Hydatula macrocephala hepatis musculi* Viborg, 1795; ? *Echinorhynchus hæruca* Lamarck, 1801; ? *E. hærucae* Bosc, 1802; *Cysticercus tæniæformis* (Batsch, 1786a) Zeder, 1803a; *C. fasciolaris* Rudolphi, 1808a; *Hydatis murina* Bosc of Lænnec, 1812; *H. hydatigena* Bosc of Lænnec, 1812; *Tænia vesicularis fasciolata* Goeze of Lamarck, 1816; *Hydatigera fasciolaris* (Rudolphi, 1808a) Lamarck, 1816; *Hydatigena fasciolaris* (Rudolphi, 1808a) Diesing, 1850a; *Hydatigena hepatis murini* Goeze of Diesing, 1850a; *Cysticercus crassicolis (fasciolaris)* Kæberlé, 1861a.

a BIBLIOGRAPHY.—For zoological discussion see Guyer, 1898a, 469–492, figs. 1–11.

margin; genital cloaca 0.05 to 0.08 mm. deep. Sexually mature segments measure 4 to 4.5 mm. long, 3 to 4.5 mm. broad; setae in vagina doubtful; ovary divided into two kidney-shaped lobes which lie distally of a transverse plane passing through



68



69

FIG. 68.—Portions of strobila of *Tania confusa*: a, anterior end, a short distance back of head; c, mature segments; f, terminal gravid segments. Natural size. (After Guyer, 1898a, fig. 1.)

FIG. 69.—Mature segment showing anatomy: lat. n., lateral nerve; ov., ovary; g. p., genital pore; r. s.; receptaculum seminis; s. g., shell gland; t., testicles; transv. c., transverse canal; ut., uterus; va., vagina, v. d., vas deferens; ventr. c., ventral canal; v. g., vitellogene gland. $\times 20$. (After Guyer, 1898a, fig. 3.)

genital pore; testicles 0.089 to 0.096 mm.; seminal vesicle present; length of cirrus pouch, 0.31 mm. Gravid (terminal) segments attain 27 to 35 mm. long by 3.5 to 5 mm. broad. Length of segments exceeds breadth in nearly entire worm. Uterus with 14 to 18 thick, short, dichotomous branches each side of median stem. Calcareous corpuscles sparse, attain 11μ . Eggs oval, 39 by 30μ .

Cysticercus: Unknown.

HABITAT.—Adult in intestine of man.

GEOGRAPHIC DISTRIBUTION.—Thus far known only for Nebraska.

MEDICAL SIGNIFICANCE.—Unknown.



FIG. 70.—Transverse section of same: *cir.*, cirrus; *cir. p.*, cirrus pouch; *cu.*, cuticle; *long. m.*, longitudinal muscles; *p. p.*, pore plug; *sag. m.*, sagittal muscles; *t. m.*, transverse muscles; *v. s.*, vesicula seminalis; other letters same as in fig. 69. $\times 40$. (After Guyer, 1898a, fig. 4.)

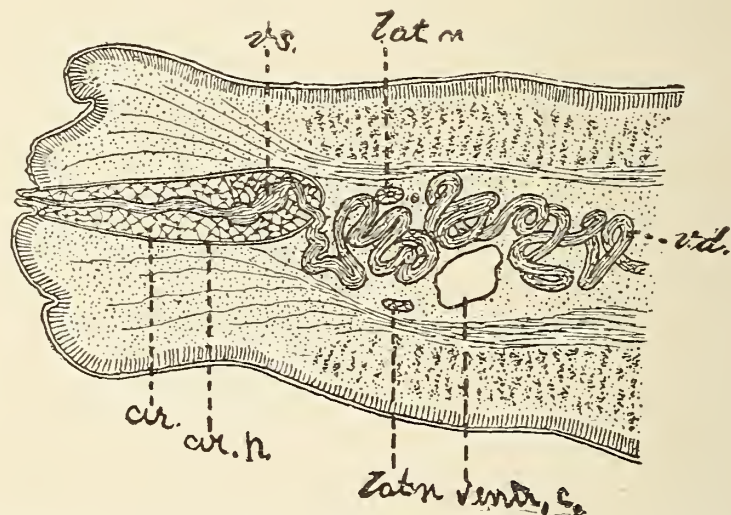
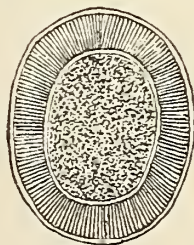


FIG. 71.—Transverse section of pore region of same: *v. s.*, vesicula seminalis; other letters same as in figs. 69 and 70. $\times 160$. (After Guyer, 1898a, fig. 7.)



72



73

FIG. 72.—Gravid segment, to show the uterus. $\times 6$. (After Guyer, 1898a, fig. 2.)

FIG. 73.—Onchosphere surrounded by embryophore, from uterus. $\times 660$. (After Guyer, 1898a, fig. 11.)

Subfamily DIPYLIDIINÆ ^a Stiles, 1896.

SUBFAMILY DIAGNOSIS.—*Teniidæ* (p. 24): Suckers unarmed. Rostellum armed, rarely absent. Genital pores marginal (lateral), single or double and opposite. Genital organs of each segment in single or double series. Uterus usually dividing up into egg sacks, or entirely disappearing so that the eggs lie free in the parenchyma. Eggs with thin transparent shells, with or without appendages. Larval forms (cysticercoides) in arthropods or mollusks. Strobila in mammals, birds, and reptiles.

TYPE GENUS.—*Dipylidium* Leuckart, 1863.

Of the genera *Dipylidium*, *Cotugnia*, *Oochoristica*, *Panceria*, *Monopylidium*, *Hymenolepis*, *Dilepis*, *Choanotænia*, *Anabotænia*, and *Nematotænia*, two groups (*Dipylidium* and *Hymenolepis*) are represented among the parasites of man.

KEY TO GENERA OF DIPYLIDIINÆ FOUND IN MAN.

Genital organs in double series; numerous testicles in each segment. *Dipylidium* (p. 48)
Genital organs in single series; 3 testicles in each segment. *Hymenolepis* (p. 51)

Genus DIPYLIDIUM ^b Leuckart, 1863.

GENERIC DIAGNOSIS.—*Dipylidiinæ*: Rostellum retractile, armed with several rings of alternating rose-thorn hooklets, which usually have a discoidal base. Suckers unarmed. Genital pores double and opposite. Genital organs in double series. Testicles very numerous, in median field. Ovary bilobed. Vitellogene glands distal of ovary. Uterus at first representing a reticulum, in the meshes of which are situated the testicles; later it breaks up into egg sacks inclosing one or several eggs. Eggs with double shell. Parasitic in mammals.

TYPE SPECIES.—*Dipylidium caninum* (Linnæus, 1758).

^a SYNONYMS.—*Rhynchotænia* Diesing, 1850a; *Malacolepidota* Weinland, 1858a; *Cystoidæ* Leuckart, 1863; *Cystoidei* Leuckart, 1886; *Cystoidotæniæ* Railliet, 1886; *Microtæniæ* Claus, 1891; *Dipylidinæ* Railliet, 1896.

^b SYNONYMS.—*Tænia* (*Dipylidium*) Leuckart, 1863; *Alyselminthus* Weinland, 1858, not Zeder, 1800; *Cryptocystis* Villot, 1882; *Microtænia* Sedgwick, 1884.

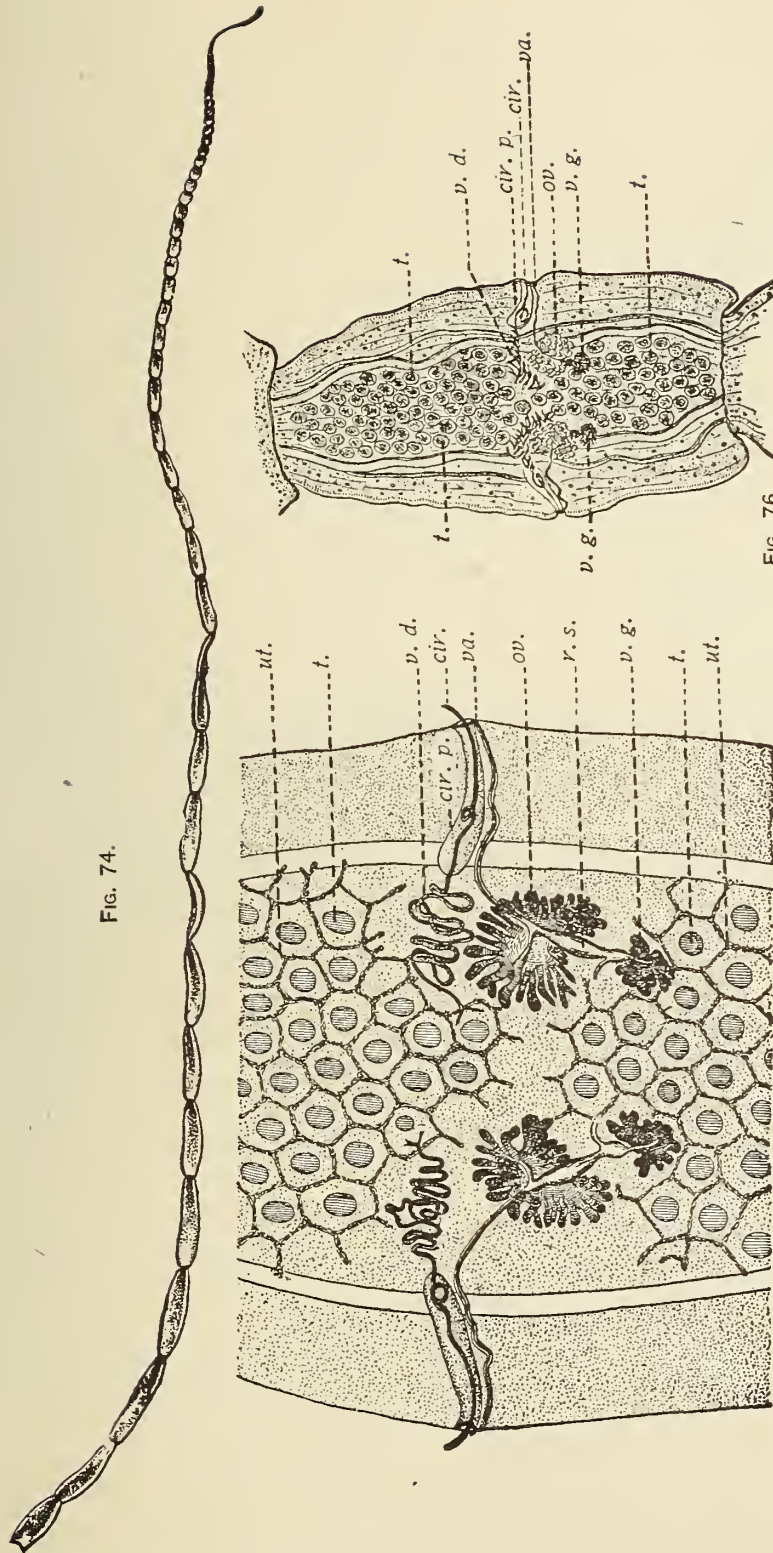


FIG. 74.

FIG. 75.

FIG. 76.

FIG. 74.—Adult strobila of the double-pored dog tapeworm (*Dipylidium caninum*). Natural size. (After Stiles, 1903, fig. 1.)
 FIG. 75.—Mature segment of same, showing the anatomy: *cir.*, cirrus (penis); *ov.*, ovary; *t.*, testis; *ut.*, uterus; *va.*, vagina; *v. g.*, vitellogene gland. × 25. (After Neumann in Railliet, 1893a, 289, fig. 188.)

FIG. 76.—Gravid segment of same; lettering same as in fig. 75. (After Diamare, 1893b, pl. 1, fig. 1.)

The Double-Pored Dog Tapeworm—*DIPYLIDIUM CANINUM*^a (Linnæus, 1758).

[Figs. 74 to 80.]

SPECIFIC DIAGNOSIS.—*Dipylidium*: Strobila 15 to 35 cm. long; head small, globular; rostellum club-shaped, with 3 to 4 rows of hooks (about 60 in number), of rose-thorn form; the anterior hooks 15μ , the posterior 6μ ; suckers, relatively large, rather elliptical. Segments 80 to 120 in number; gravid segments 8 to 11 mm. long, 1.5 to

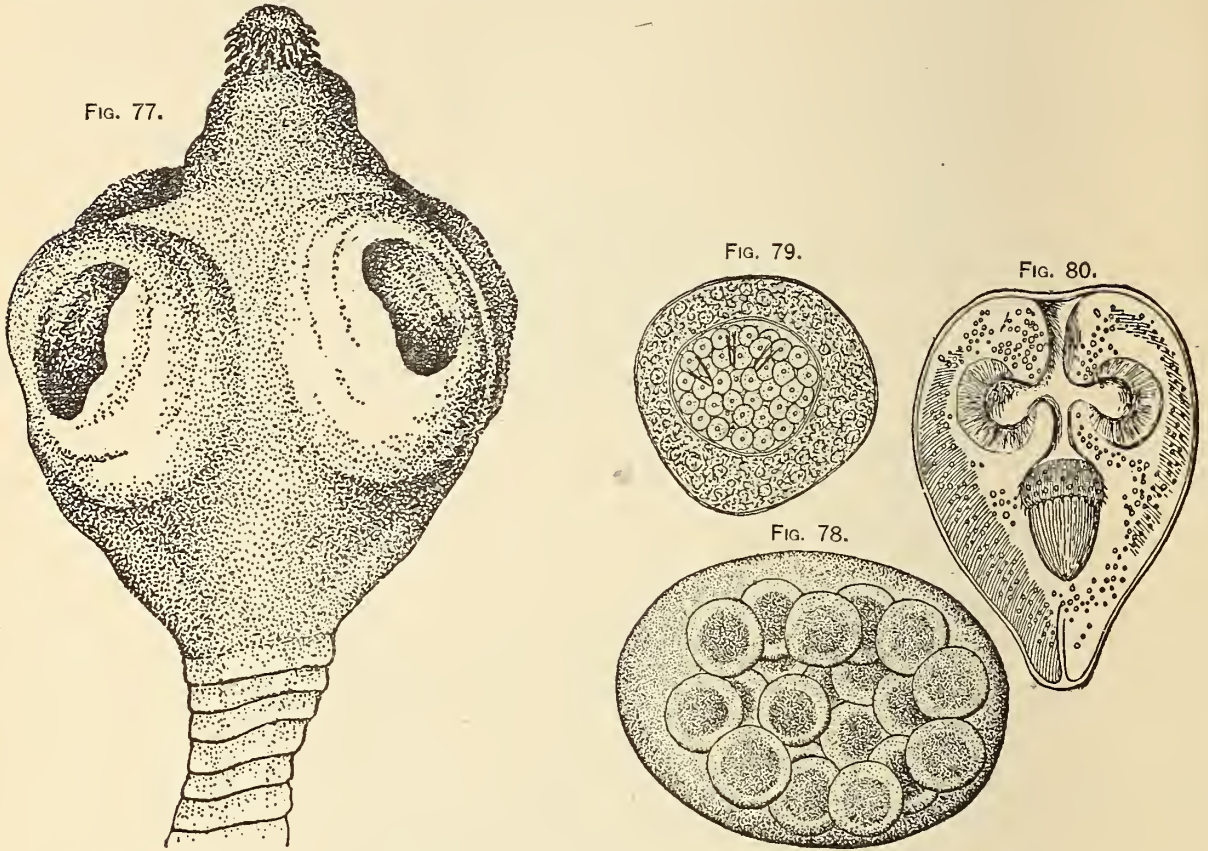


FIG. 77.—Head of same, showing four rows of rose-thorn hooks on the rostellum and four unarmed suckers. Greatly enlarged. (After Stiles, 1903, fig. 4.)

FIG. 78.—Egg packet of same, greatly enlarged. (After Stiles, 1903, fig. 5.)

FIG. 79.—Egg of same. Note the six hooks in the embryo. Greatly enlarged. (After Stiles, 1903, fig. 6.)

FIG. 80.—*Cryptocystis trichodectis*, the cystic (infecting) stage of *Dipylidium caninum*, as found in the flea. (After Leuckart, 1886, 847, fig. 348.)

3 mm. broad, often reddish in color. Genital pores at equator or in posterior half of segment; uterus forms egg capsules, each containing 8 to 20 eggs; eggs globular, 43 to 50μ in diameter; egg shell thin; onchosphere 32 to 36μ .

HABITAT.—Adults in small intestine of dogs (*Canis familiaris*) and cats (*Felis catus*); occasionally as accidental parasite in man. Larvæ in lice (*Trichodectes canis*) and fleas (*Ctenocephalus canis* and *Pulex irritans*).

GEOGRAPHIC DISTRIBUTION.—Probably more or less cosmopolitan.

^a**SYNONYMS.**—*Tænia canina* Linnæus, 1758a; *T. moniliformis* Pallas, 1781 (not Batsch, 1786a); *T. cucumerina* Bloch, 1782a; *T. cateniformis* Gœze, 1782a; *T. elliptica* Gœze, 1782a; *T. elliptica* Batsch, 1786a; *T. moniliformis* Schrank, 1788; *T. cateniformis canina* Linnæus of Gmelin, 1790a; *T. cateniformis felis* Gmelin, 1790a; *Alyselminthus ellipticus* (Batsch, 1786a) Zeder, 1800a; *Halysis elliptica* (Batsch, 1786a) Zeder, 1803a; *Tænia canina* (Linnæus, 1758a) Beneden, 1861a; *T. cucumerina* (Bloch, 1782a) Beneden, 1861a; *Tænia* [(*Dipylidium*)] *cucumerina* Bloch of Leuckart, 1863; *Cryptocystis trichodectis* Villot, 1882; *Dipylidium caninum* (Linnæus, 1758a) Railliet, 1893a.

BIBLIOGRAPHY.—See Diamare, 1893b.

MEDICAL SIGNIFICANCE.—Probably a purely accidental parasite for man, more likely to occur in children. The worms have a tendency to burrow into the intestinal mucosa, making a tunnel-like channel, through which the segments are pulled much like a train of cars passing through a tunnel.

PREVENTION.—Children should not be allowed to play with dogs and cats that are infested with fleas and lice.

Genus HYMENOLEPIS^a Weinland, 1858.

GENERIC DIAGNOSIS.—*Dipylidiinae* (p. 48): Head generally small; rostellum retractile well developed and armed, or rudimentary and unarmed; suckers usually unarmed. Genital pores single, marginal, unilateral. Testes few; usually three in each segment. Uterus saclike; often filling the segment; frequently with outpocketings and incomplete partitions. Eggs with two, three, or four membranes, the inner of which closely invests the embryo and may exhibit a small mammillate projection at each pole; the outer membrane is separated from the inner by a wide intervening space. Larva a cercocyst or staphylocyst.

TYPE SPECIES.—*Hymenolepis flavopunctata* Weinland, 1858 = *H. diminuta* (Rudolphi, 1819).

KEY TO THE SPECIES OF HYMENOLEPIS REPORTED FOR MAN.

(For species thus far found in man in the United States, follow roman type.)

Strobila small, 5 to 45 mm. long by 0.5 to 0.9 mm. wide, filiform; head armed with a crown of 20 to 30 hooks; eggs generally oval, with filaments attached to the poles of the inner membrane; common. *Hymenolepis nana* (p. 51)

Strobila 10 to 60 mm. long by 2.5 to 4 mm. wide; head unarmed; eggs generally round, prominent intermediate layer of albuminous substance between outer and inner membranes, outer membrane frequently with radial striations; rare in man..... *Hymenolepis diminuta* (p. 54)

Strobila lanceolate, 30 to 130 mm. long by 5 to 18 mm. broad; head small, compared with strobila, armed with 8 to 10 hooks; eggs oval, without filaments on the inner membrane; very rare in man *Hymenolepis lanceolata* (p. 58)

The Dwarf Tapeworm—HYMENOLEPIS NANA^b (Siebold, 1852) Blanchard, 1891.

[Figs. 81 to 87.]

SPECIFIC DIAGNOSIS.—*Hymenolepis* (p. 51): Strobila 5 to 45 mm. in length, 0.5 to 0.9 mm. in maximum breadth, composed of about 100 to 200 segments. Head subglobular, 130 to 480 μ in diameter; rostellum well developed, freely movable, armed with a single crown of 20 to 30 hooks, 14 to 18 μ in length; suckers globular, 80 to 150 μ in diameter. Neck long. Anterior segments very short; following segments

^a **SYNONYMS.**—*Hymenolepis* Weinland, 1858; *Diplocanthus* Weinland, 1858 (not Agassiz, 1842, fish); *Lepidotrias* Weinland, 1858; "*Hymenolepsis*" of Osler, 1895, and other authors (misprint); "*Diplocanthus*" of Cohn, 1899 (misprint).

^b **SYNONYMS.**—*Tænia murina* Dujardin, 1845a (not *T. murina* Gmelin, 1790a = *Cysticercus fasciolaris* Rudolphi); *Tænia nana* Siebold, 1852, not (van Beneden, 1858) Diesing, 1864a; *T. ægyptiaca* Bilharz, 1852, not Krabbe, 1869; *T. nana* Kuechenmeister, 1855, misprint for *nana*; *Diplocanthus nanus* (Siebold, 1852) Weinland, 1858; *Tænia* (*Hymenolepis*) *nana* Siebold of Leuckart, 1863; *T. "rana"* of Bell, 1886b (misprint); *Hymenolepis nana* Blanchard, 1891a; *H. murina* Blanchard, 1891a; "*Hymenolepsis*" *nana* of Osler, 1895, and other authors (misprint); *Tænia "minima"* of Huber, 1896a (misprint for *T. murina*).

BIBLIOGRAPHY.—For medical and zoological discussion of this species, with compilation of 106 cases, see Ransom, 1904.

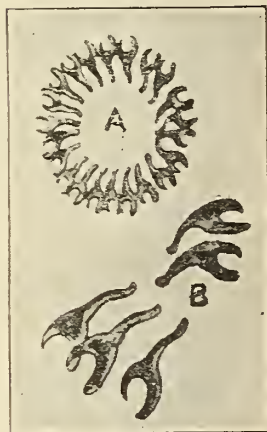
increase in length and breadth, but remain broader than long, except that the length of the hindermost segments may occasionally equal or even slightly exceed their breadth. Genital pores on the left margin, near anterior border of each segment. Three testes in each segment; vas deferens enlarged to form a seminal vesicle within the cirrus pouch, while a seminal reservoir outside the cirrus pouch is only slightly developed or absent. Gravid uterus occupies nearly the entire segment; wall of uterus with a few inconspicuous infoldings, forming incomplete partitions extending



81



82



83

FIG. 81.—Head and strobila of dwarf tapeworm (*Hymenolepis nana*). Enlarged. (After Leuckart, 1863, 393, fig. 112.)

FIG. 82.—Head of dwarf tapeworm (*H. nana*). Enlarged. (After Leuckart, 1863, 394, p. 113.)

FIG. 83.—Hooks of *Hymenolepis nana*: a, complete crown; b, isolated hooks. Enlarged. (After Krantz, from Kuechenmeister & Zuern, 1881a, pl. 5, fig. 4.)

into the cavity of the uterus. Eggs number 80 to 180 in each segment; oval or globular; two distinct membranes; outer membrane 30 to 60 μ in diameter; inner membrane 16 to 34 μ in diameter, presenting at each pole a more or less conspicuous mammillate projection, provided with filamentous appendages; embryonal hooks 10 to 14 μ long.

HABITAT. *a*.—Small intestine of brown or Norway rat (*Mus decumanus*), black rat (*Mus rattus*), dwarf field mouse (*Mus minutus*), house mouse (*Mus musculus*), garden dormouse (*Eliomys quercinus*), and man (*Homo sapiens*).

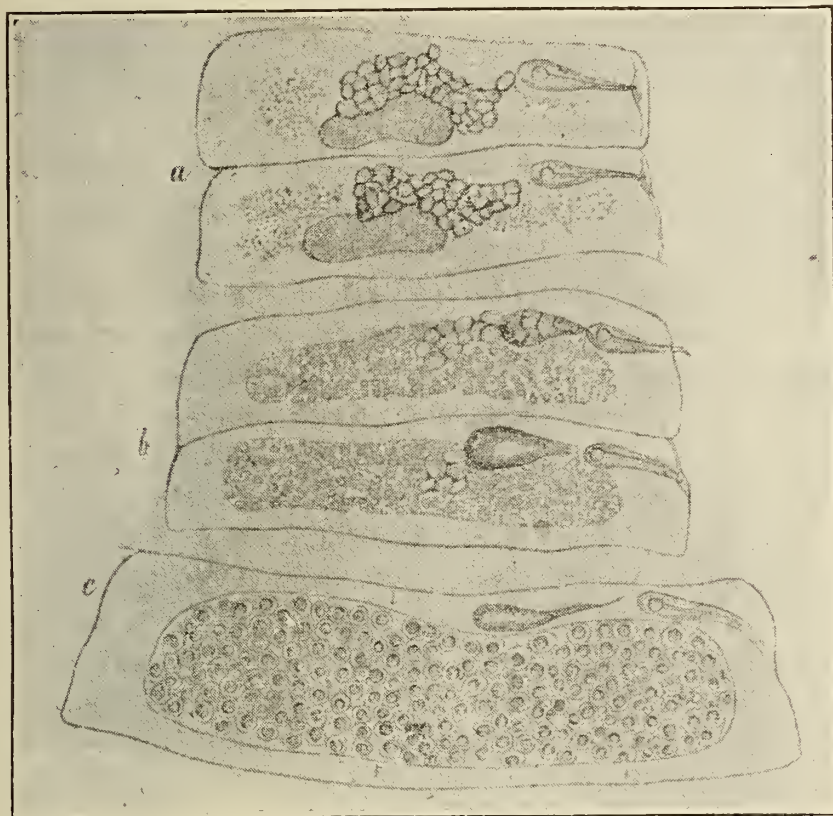
a There is some slight doubt as yet as to the absolute identity of the parasite in man with that of rodents, but from a standpoint of prevention they should at present be considered identical. The form in the rat (type host *Mus decumanus*, in France) may at least be viewed as a host subspecies (*H. nana fraterna* Stiles, 1906).

DEVELOPMENT.—The embryo is swallowed, and after hatching enters a villus of the small intestine, where it transforms into a cercocystis, which in turn falls into the lumen of the intestine and becomes adult.

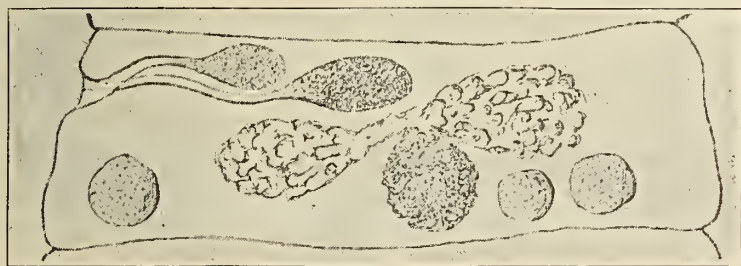
GEOGRAPHIC DISTRIBUTION.—Egypt, England, Italy, Sicily, Russia, Germany, Serbia, France, Austria, Denmark, Siam, Japan, Pennsylvania, District of Columbia, Maryland, South Carolina, Georgia, Texas, Brazil, and Argentina.

MEDICAL SIGNIFICANCE.—This parasite is more or less common, particularly in children in warmer climates. Treatment: male fern.

PREVENTION.—If a patient harbors this tapeworm he should not be allowed to sleep in the same bed with another person. Personal cleanliness, especially after defecation.



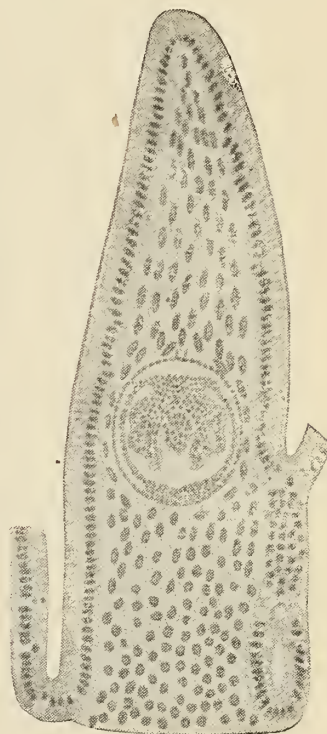
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85



86



87

FIG. 84.—Proglottids of *Hymenolepis nana*: *a*, showing ovary; *b*, containing eggs in course of formation; *c*, gravid segment. Enlarged. (After Leuckart, 1863, 396, fig. 114.)

FIG. 85.—Segment of *Hymenolepis nana* showing three testicles, two ovaries, etc. Enlarged. (After Leuckart, 1886, fig. 409a.)

FIG. 86.—Egg of *Hymenolepis nana* as seen in fresh feces. Enlarged. (After Ransom, from Stiles, 1903, 85, fig. 85.)

FIG. 87.—Longitudinal section of the intestinal villus of a rat, containing cystic stage of dwarf tapeworm. Enlarged. (After Grassi & Rovelli, 1892a, pl. 3, fig. 25.)

The Yellow Spotted Tapeworm—*HYMENOLEPIS DIMINUTA*^a (Rudolphi, 1819) Blanchard, 1891.

[Figs. 88 to 95.]

SPECIFIC DIAGNOSIS.—*Hymenolepis* (p. 51): Strobila 10 to 60 mm. in length, 2.5 to 4 mm. in maximum breadth; composed of 800 to 1,300 segments. Head small, almost globular; 200 to 600 μ in width; rostellum rudimentary, pyriform, only slightly protractile; hooks absent; suckers globular, near the apical portion of the head, 80 to 160 μ in diameter. Neck usually short. Segments throughout strobila broader than long. Genital pores on left margin, near the junction of the anterior and middle thirds of each segment. Three testes in each segment; vas deferens dilates into a prominent seminal vesicle before entering the cirrus pouch, within which also is a vesicle. Gravid uterus occupies most of the proglottids; its cavity is subdivided into a large number of incompletely separated compartments filled with eggs. Eggs round or slightly oval; outer membrane 54 to 86 μ in diameter, yellowish in color, may be radially striated; inner membrane 24 by 20 μ to 40 by 35 μ in diameter, with mammillate projection at each pole often not apparent; between outer and inner membranes a prominent third layer of albuminous substance, often appearing as two delicate smooth membranes, with intervening space filled by a granular coagulum; embryonal hooks 11 to 16 μ in length.

HABITAT.—Adults in small intestine of brown or Norway rat (*Mus decumanus*), black rat (*M. rattus*), house mouse (*M. musculus*), Egyptian or roof rat (*M. rattus alexandrinus*), wood or field mouse (*M. sylvaticus*), *Rhipidomys pyrrhorhinus* [according to Linstow, 1878a, 23], and man (*Homo sapiens*).

DEVELOPMENT.—The larval stage (*Cercocystis H. diminuta*) occurs in larval and adult meal moths (*Asopia farinalis*); in young and adult earwigs (*Anisolabis annulipes*); and in adult beetles (*Acis spinosa* and *Scaurus striatus*).

GEOGRAPHIC DISTRIBUTION.—Massachusetts, Pennsylvania, Nebraska, Iowa, District of Columbia, Maryland, Brazil, Italy, Germany, France, Austria.

MEDICAL SIGNIFICANCE.—A rare and probably accidental parasite of man; easily expelled.

^aSYNONYMS.—*Tenia diminuta* Rudolphi, 1819a; *T. leptocephala* Creplin, 1825a; *Hymenolepis flavopunctata* Weinland, 1858; *Tenia (Hymenolepis) flavopunctata* Weinland, 1859; *H. (Lepidotrias) flavopunctata* Weinland, 1861; *T. flavomaculata* Leuckart, 1863; *T. "flavopuncta"* Cobbold, 1864b (misprint); *T. "flaviopunctata"* Vogt, 1878 (misprint); *T. "flavopunktata"* Stein, 1882; *T. ravesina* E. Parona, 1884; *T. minima* Grassi, 1886; *T. "septocephala"* Perroncito & Airoidi, 1888 (misprint); *Hymenolepis diminuta* (Rudolphi, 1819) Blanchard, 1891a; "*Hymenolepsis*" *flavopunctata* of Osler, 1895, and other authors (misprint); *T. "raverina"* Huber, 1896a (misprint for *T. ravesina*); *T. "flarapunctata"* Simon, 1896 (misprint); *T. "leptocephala"* Previtera, 1900; *T. "ceptocephala"* Lussana & Romaro [? date] (misprint); *Tenia flavopunctata* (Weinland, 1858) Packard, 1900.

BIBLIOGRAPHY.—For medical and zoological discussion of this species, with compilation of 10 cases, see Ransom, 1904.

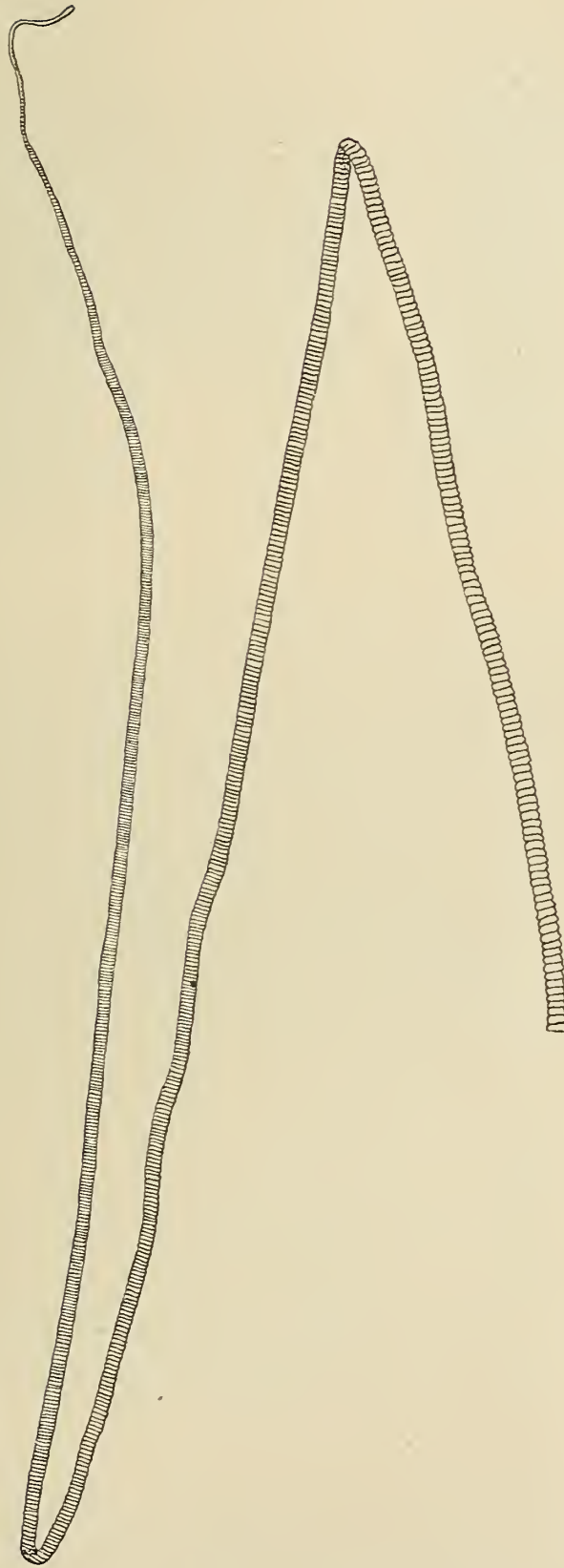
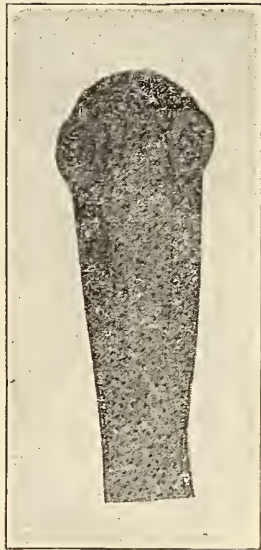


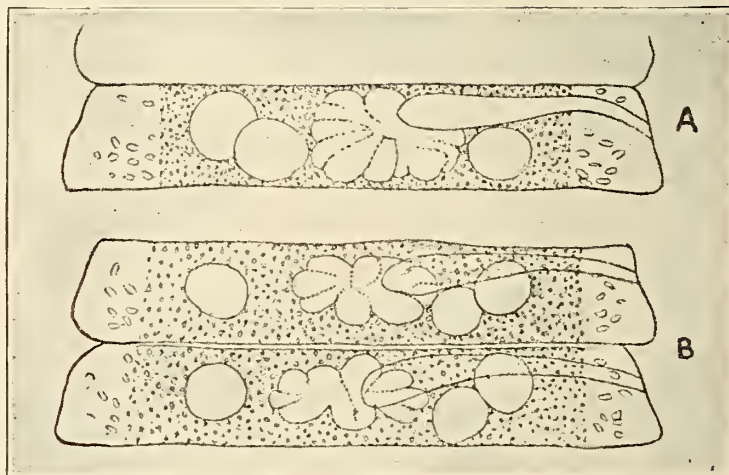
FIG. 88.—Strobila of *Hymenolepis diminuta*. Natural size. (After Grassi, 1888l, pl. 11, fig. 1.)



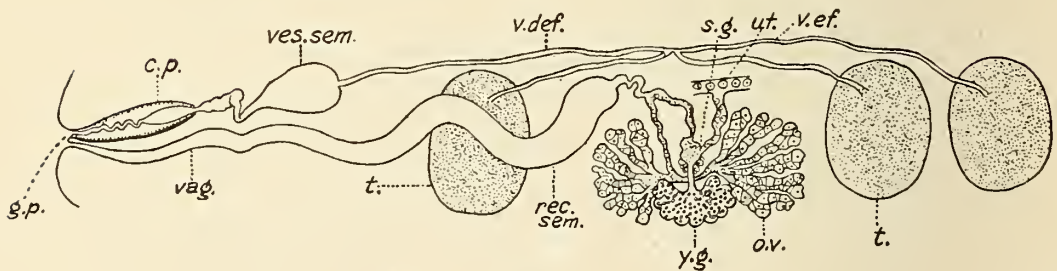
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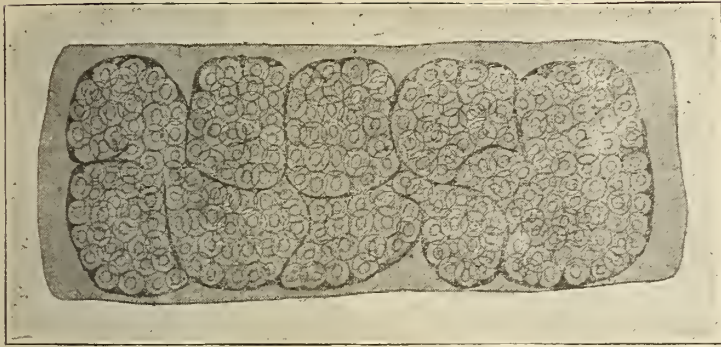
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FIG. 89.—Head and neck of *H. diminuta* from man. Enlarged. (After E. Parona, 1884, fig. 4.)

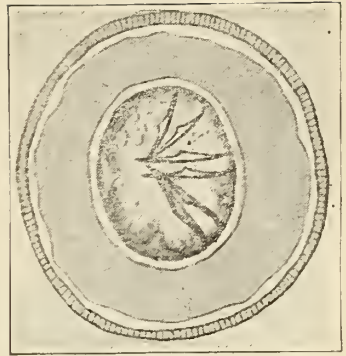
FIG. 90.—Head and anterior portion of *H. diminuta* from the rat. Enlarged. (After Zschokke, 1889, pl. 1, fig. 21.)

FIG. 91.—Segments of *H. diminuta* showing the usual (A) and unusual (B) position of testes. Enlarged. (After Grassi, 18881, pl. 11, fig. 14.)

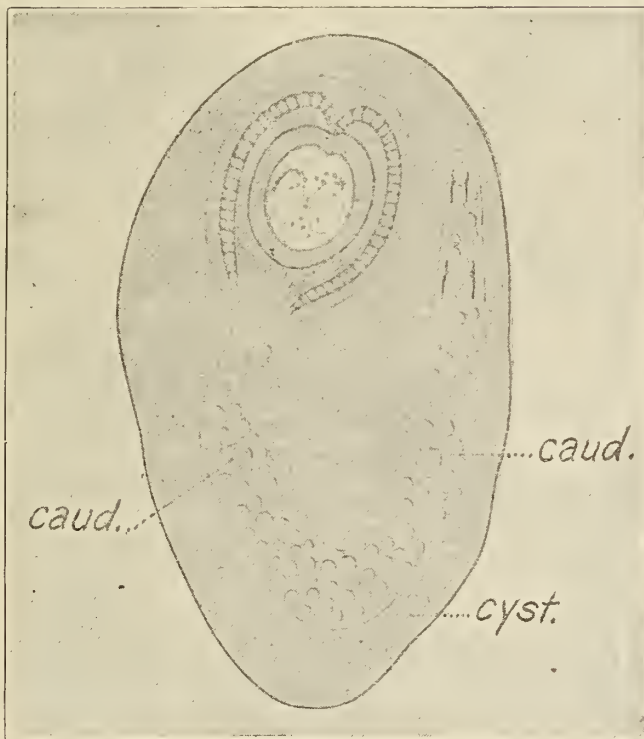
FIG. 92.—Male and female organs of *H. diminuta*: *c. p.*, cirrus pouch; *g. p.*, genital pore; *ov.*, ovary; *rec. sem.*, receptaculum seminis; *s. g.*, shell gland; *t.*, testes; *ut.*, uterus; *vag.*, vagina; *v. def.*, vas deferens; *v. ef.*, vas efferens; *ves. sem.*, vesicula seminalis; *y. g.*, yolk gland. Enlarged. (After Zschokke, 1889, pl. 2, fig. 22.)



93



94



95

FIG. 93.—Gravid segment of *H. diminuta*. Enlarged. (After Grassi, 1888l, pl. 11, fig. 15.)

FIG. 94.—Egg of *H. diminuta* from man. Greatly enlarged. (After Bizzozzero, 1889a, pl. 4, fig. g".)

FIG. 95.—Encysted cystic stage of *H. diminuta*: *caud.*, caudal appendage; *cyst.*, adventitious capsule inclosing the cercocystis. Enlarged. (After Grassi & Rovelli, 1892a, pl. 4, fig. 1.)

The Lanceolate Tapeworm—*HYMENOLEPIS LANCEOLATA*^a (Bloch, 1782)
Weinland, 1858.

[Figs. 96 to 100.]

SPECIFIC DIAGNOSIS.—*Hymenolepis* (p. 51): Strobila lanceolate, 30 to 130 mm. long by 5 to 18 mm. broad. Head, compared with strobila, very small; rostellum protractile, armed with single row of 8 hooks, 31 to 35 μ long. Neck short, often retracted with head into anterior portion of strobila. Segments much broader than long throughout the strobila. Genital pores on right-hand margin of segment near anterior border. Three testes in each segment; vas deferens enlarged to form a seminal vesicle, frequently S-shaped, before entering cirrus pouch; within latter a second vesicle; vas deferens describes a complete loop in cirrus pouch before being transformed into the cirrus; cirrus freely protrusible, armed with spines. Female organs on opposite side of segment from genital pore; gravid uterus sac-like, with out-pocketings, filling most of the segment. Egg oval or spherical, with two thin membranes separated by an intervening space containing a small amount of albuminous substance; inner membrane occasionally with polar papillæ; outer membrane 50 by 35 μ to 100 by 100 μ in diameter; inner membrane 30 by 25 μ to 40 by 25 μ in diameter; embryonal hooks 8 to 15 μ in length.

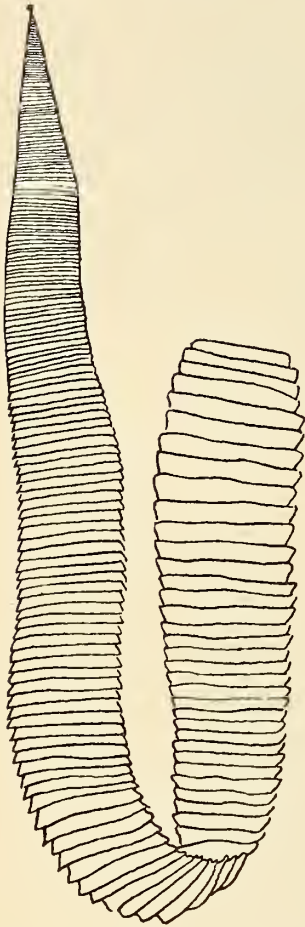


FIG. 96.—Head and strobila of *Hymenolepis lanceolata*. Natural size. (After Goetze, 1782a, pl. 29, fig. 23.)

flamingo (*Phoenicopterus roseus*). Zschokke (1902) has recently reported one case in man (*Homo sapiens*).

DEVELOPMENT.—Not experimentally determined. Larval stage probably lives in small fresh-water crustacea.

GEOGRAPHIC DISTRIBUTION.—England, Denmark, France, Germany, and Austria.

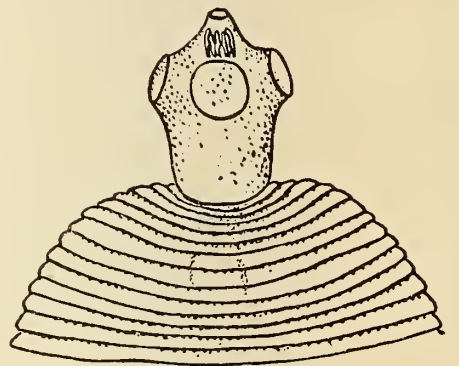
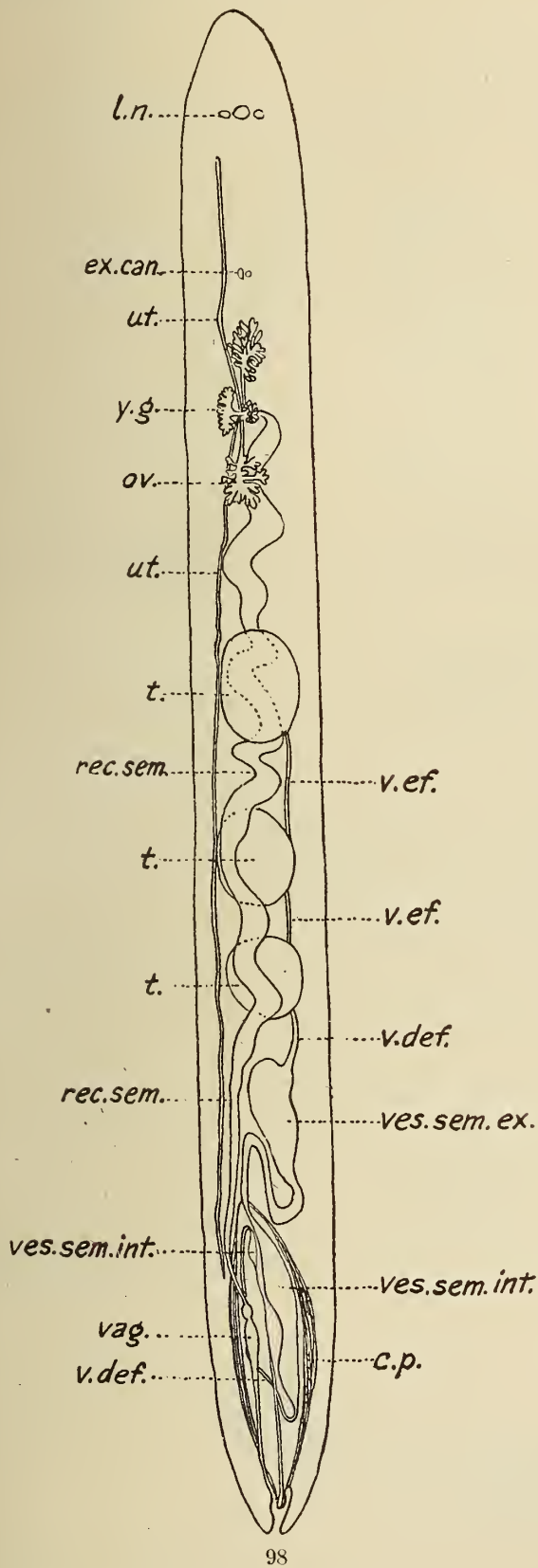


FIG. 97.—Head with retracted rostellum and anterior portion of *H. lanceolata*. Enlarged. (After Railliet, 1886, 267, fig. 163a.)

^aSYNONYMS.—*Tenia anserum* Frisch, 1727 [according to Rudolphi, 1810a]; *T. anseris* Bloch, 1779 [according to Rudolphi, 1810a]; *T. lanceolata* Bloch, 1782a (not *T. lanceolata* Chabert; not *T. lanceolata* Rosseter, 1891); *T. acutissima* Pallas, 1781, in part; *T. lanceola* Batsch, 1786a; *Halysis lanceolata* (Bloch, 1782) Zeder, 1803a; *Hymenolepis* (*Dilepsis*) *lanceolata* (Bloch, 1782) Weinland, 1858; *Drepanidotenia lanceolata* (Bloch, 1782) Railliet, 1892; *Hymenolepis* (*Drepanidotenia*) *lanceolata* (Bloch, 1782) Cohn, 1899; *Tenia-Drepanidotenia lanceolata* (Bloch, 1782) Dadai, 1900a.

BIBLIOGRAPHY.—For medical and zoological discussion, see Ransom, 1904.

MEDICAL SIGNIFICANCE.—An accidental parasite in man; only one case has been recorded.



99



100

FIG. 98.—Transverse section of segment of *H. lanccolata*: *c. p.*, cirrus pouch *ex. can.*, excretory canals; *l. n.*, lateral longitudinal nerves; *ov.*, ovary; *rec. sem.*, receptaculum seminis; *t.*, testis; *ut.*, uterus; *vag.*, vagina; *v. def.*, vas deferens; *v. ef.*, vas efferens; *ves. sem. ex.*, vesicula seminalis externa; *ves. sem. int.*, vesicula seminalis interna; *y. g.*, yolk gland. Enlarged. (After Wolffhugel, 1900b, 51, fig. 2.)

FIG. 99.—Egg of *H. lanccolata*. Enlarged. (After Railliet, 1886, 267, fig. 163b.)

FIG. 100.—Supposed cystic stage of *H. lanccolata*. Enlarged. (After Dadai, 1900a, pl.10, fig. 9.)

Subfamily DAVAINÆINÆ Braun, 1900.

SUBFAMILY DIAGNOSIS.—Tæniidæ (p. 24): Rostellum and suckers armed with hooks. Genital pores irregularly alternate or unilateral. Genital organs in single series. Eggs usually in egg-capsules. Parasites of mammals and birds.

TYPE GENUS.—*Davainea* Blanchard, 1891.

Of the genera *Davainea*, *Echinocotyle*, and *Ophryocotyle*, only *Davainea* occurs in man.

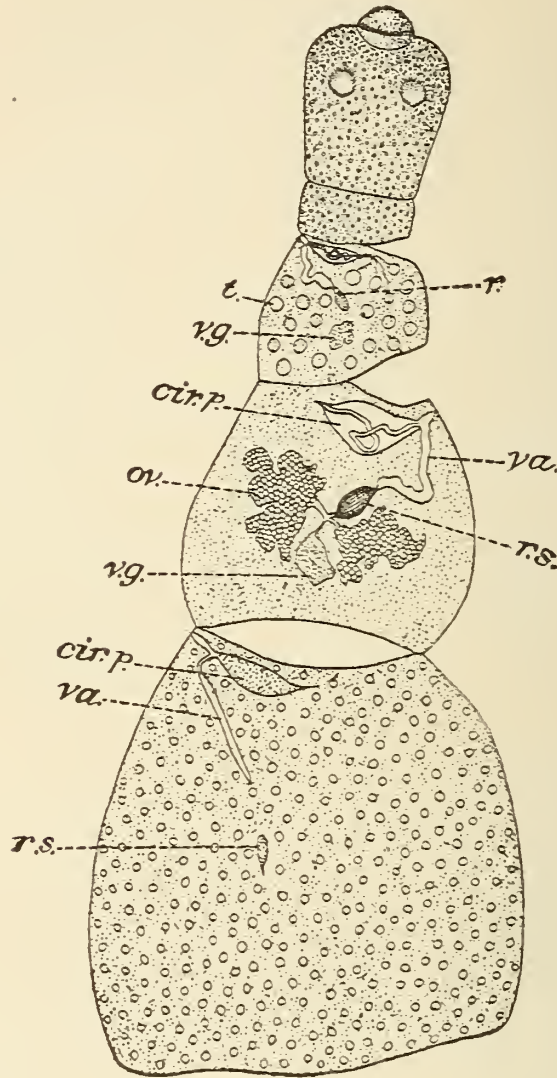


FIG. 101.—*Davainea proglottina*, type of genus, enlarged 95 times to show the anatomy: *cir. p.*, cirrus pouch; *ov.*, ovary; *r. s.*, receptaculum seminis; *t.*, testicles; *va.*, vagina; *v. g.*, vitellogene gland. (After Blanchard, 1891t, 430, fig. 4.)



FIG. 102.—A portion of the double row of hooks on the rostellum of *Davainea salmoni* of rabbits. Greatly enlarged. (After Stiles, 1896n, pl. 23, fig. 6.)

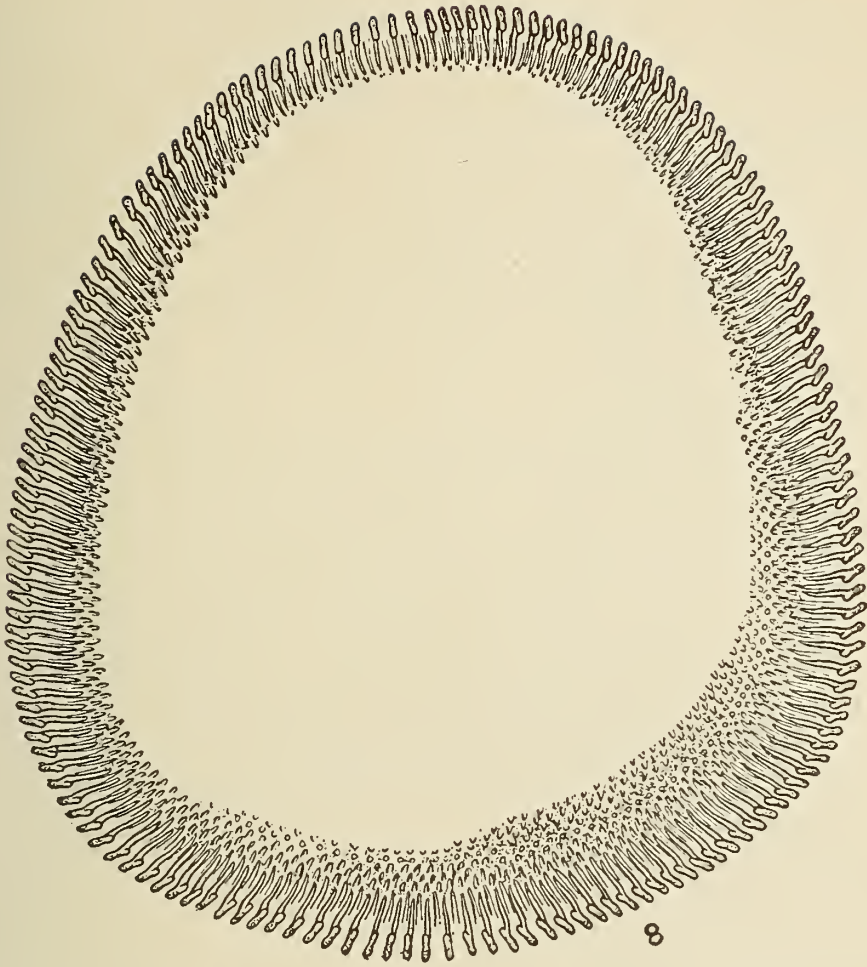


FIG. 103.—View of the hooks on a sucker of *Davainea salmoni* of rabbits. Greatly enlarged. (After Stiles, 1896n, pl. 23, fig 8.)

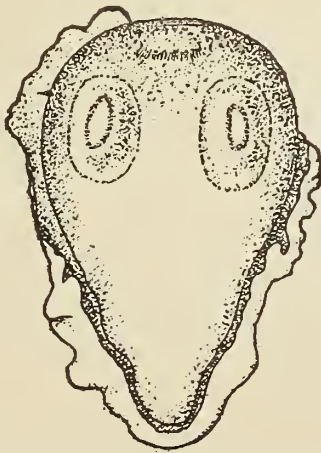


FIG. 104.—A very young *Davainea salmoni*, still partially surrounded by a cyst, and showing armed rostellum and suckers; from the cottontail rabbit. Greatly enlarged. (After Stiles, 1896n, pl. 25, fig. 10.)

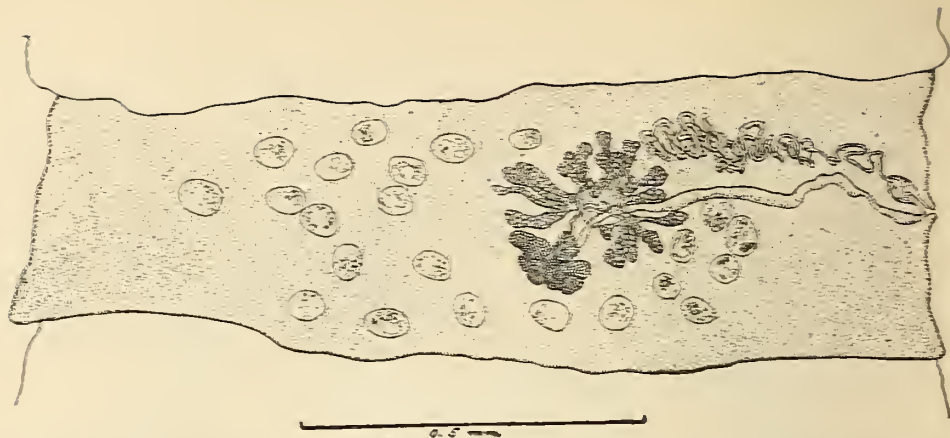


FIG. 105.—Segment of *Davainea tetraena* of chickens, enlarged to show the reproductive organs. (After Ransom, 1904, 61, fig. 17.)

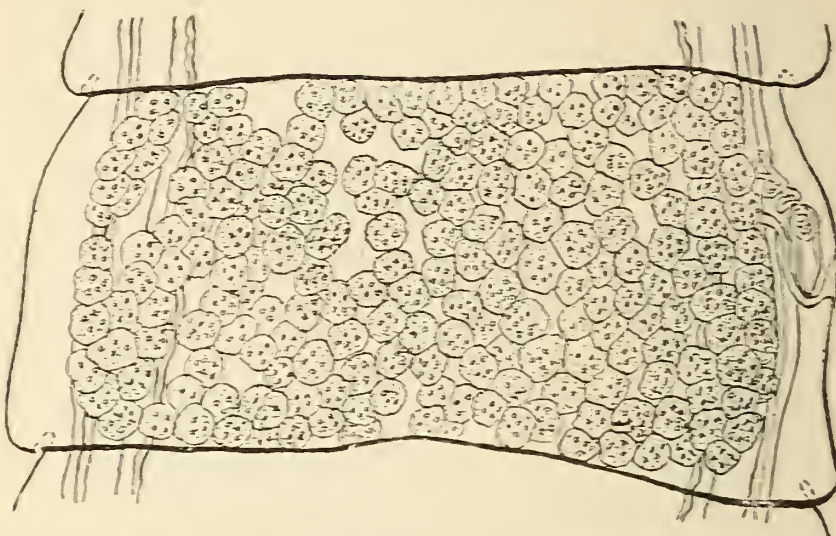


FIG. 106.—Gravid segment of *Davainea salmoni* of the cottontail rabbit, enlarged dorsal view showing longitudinal nerves and canals, cirrus pouch, vagina, and numerous egg capsules. (After Stiles, 1896, pl. 22, fig. 4.)

Genus DAVAINEA^a Blanchard & Railliet, 1891.

GENERIC DIAGNOSIS.—*Davaineinae* (p. 60): Scolex with a rostellum armed with numerous hammer-shaped hooklets, arranged in two rows. Suckers with several rings of small hooklets. Genital pores usually unilateral, less frequently irregularly alternate. Eggs in egg capsules, in nearly the entire middle field of the segments. Parasitic in mammals and birds. Larval form (a cysticercoid) in mollusks and arthropods.

TYPE SPECIES.—*Davainea proglottina* (Davaine, 1869).

The two species of this genus reported for man (neither of them known yet for North America) may be distinguished by the following key:

- | | |
|--|------------------------------------|
| <i>Testicles</i> 50 or more in each segment; 500 to 400 egg balls in each gravid segment; calcareous corpuscles present..... | <i>D. madagascariensis</i> (p. 63) |
| <i>Testicles</i> 14 to 15 on each transverse section, arranged in single ventral and dorsal rows; 60 to 80 egg balls in each gravid segment; calcareous corpuscles absent..... | <i>D. asiatica</i> (p. 65) |

^aSYNONYM.—? *Liga* Weinland, 1857, type, *punctata*; ?? *Chapmania* Monticelli, 1893, type *Tenia argentina*. In case of a division of the genus *Davainea*, the species reported for man will not remain in *Davainea* s. str.

The Madagascar Tapeworm—*DAVAINEA MADAGASCARIENSIS*^a (Davaine, 1869) Blanchard, 1891.

[Figs. 107 to 108.]

SPECIFIC DIAGNOSIS.—*Davainea* (p. 62): Strobila attains 25 to 30 cm. in length by 1.4 mm. in breadth, and is composed of 500 to 600 segments, of which the last 100 are gravid and form one-half of the total length of the worm. Head with 4 large, round suckers; rostellum retractile, 0.1 mm. in diameter, plump, with 90 peculiar hooks (18 μ long) at its equator; the inner surface of the rostellum-pouch provided with numerous minute points, which are found also on the inner surface of the suckers. Proximal segments broader than long; gravid segments become longer than broad (2 by 1.4 mm.) and resemble apple seeds in shape; the distal 100 segments compose about one-half of the entire worm. Calcareous corpuscles present. Sexual development very rapid, so that segments 3 cm. from head are in copula. Genital pores unilateral, near proximal corner of segment; genital cloaca deep. *Male* organs: Cirrus pouch bottle-shaped; ductus ejaculatorius very long and sinuous, provided with prostatic gland-cells; testicles numerous, 50 or more. *Female* organs: Receptaculum seminis unusually long and broad, extending to median line of segment and communicating with oviduct; shell-gland included in the vitelloduct; uterus composed of a number of tubes which roll up each side in a nearly globular ball; when uterus is filled with eggs, the windings of the uterus unroll, extend throughout the segment, and lose their walls, so that the eggs now lie free in the parenchyma; the eggs then become surrounded, singly or 2 or 3 together, by parenchymatic cells, forming egg-balls, of which 300 to 400 are present. Onchosphere (8 μ to 15 μ) is surrounded by 2 clear shells, the outer bearing 2 mammillate projections.

Larval stage unknown; probably in some invertebrate. Blanchard suggests that cockroaches (*Blatta orientalis*) may possibly be the intermediate host.

HABITAT.—Adult in intestine of man, chiefly children.

GEOGRAPHIC DISTRIBUTION.—Tropical regions of Old and New World, possibly more common

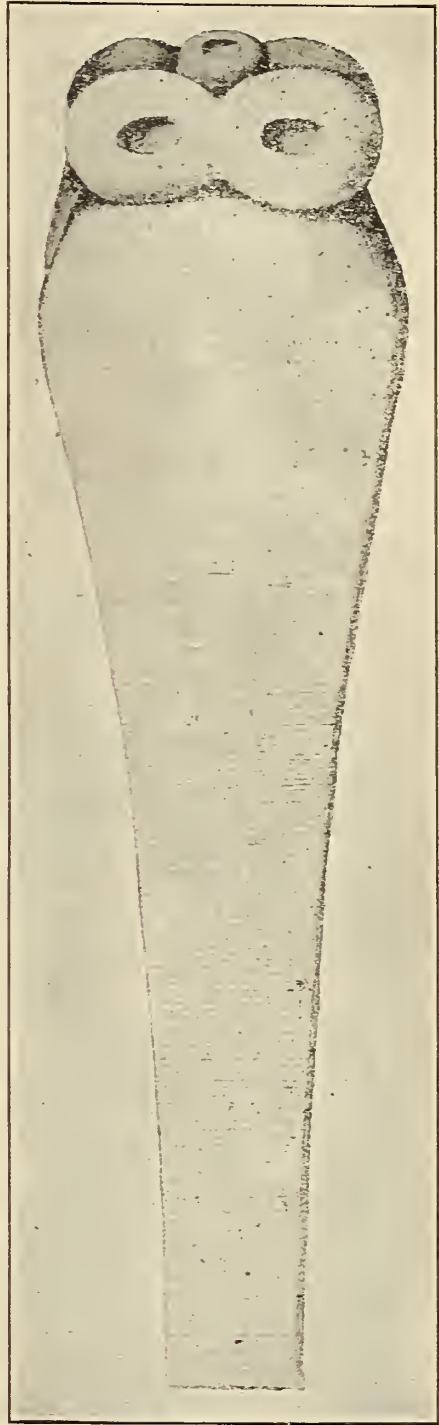


FIG. 107.—Head and anterior portion of *Davainea madagascariensis*; the hooks have fallen from the specimen. $\times 27$. (After Blanchard, 1899d, 202, fig. 1.)

^aSYNONYMS.—*Tænia madagascariensis* Davaine, 1870c; *T. demerariensis* Daniels, 1895d.

BIBLIOGRAPHY.—For list of cases see Blanchard, 1899d.

than assumed at present. Thus far reported in 9 or 10 cases, from Mayotte (Comoro Islands, by Grenet), Port Louis (Mauritius Island, by Chavereau), Nossi-bé Island (Davaine Collection, reported by Blanchard), and Georgetown (British Guiana, by Daniels).

MEDICAL SIGNIFICANCE.—Unknown.

PREVENTION.—Unknown.

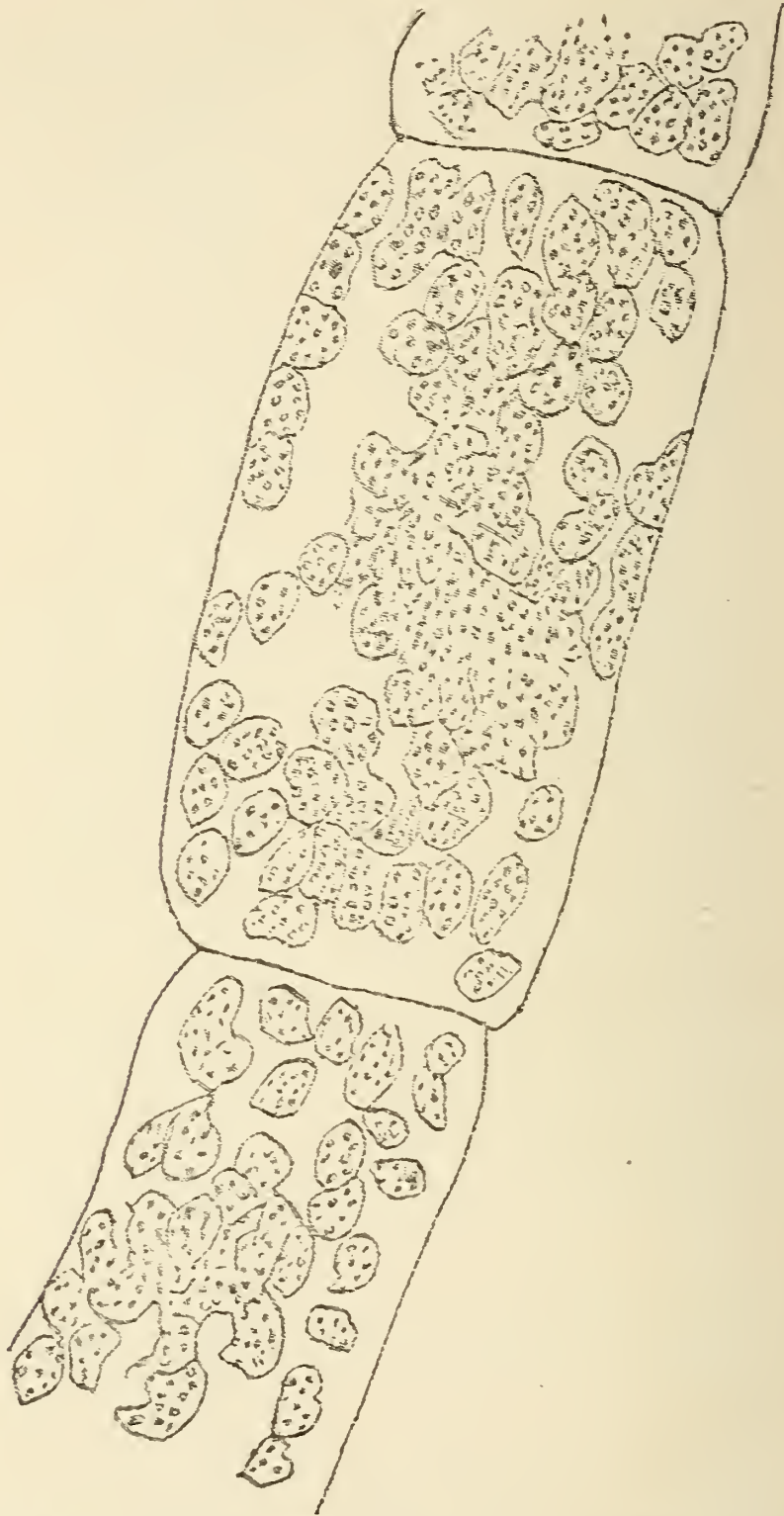


FIG. 108.—Gravid segment of *Tania dentariensis* equals *Davainea madagascariensis*, showing the egg balls. Enlarged. (After Daniels, 1895d.)

The Asiatic Tapeworm—*DAVAINEA ASIATICA* ^a (Linstow, 1901).

[Figs. 109 to 113.]

SPECIFIC DIAGNOSIS.—*Davainea* (p. 62): Length 29.8 cm., maximum breadth 1.276 mm., composed of about 750 segments. Head unknown. Segments all broader than long, varying in size from the anterior to the terminal as follows: 0.16 mm.; 0.67 by 0.32 mm.; 1.056 by 0.352 mm.; 1.276 by 0.88 mm.; 1.78 by 0.99 mm.; thickness, 0.238 in middle segments to 0.484 mm. in terminal segments; the distal margin of each segment extends over the proximal margin of the next following segment. Cortical layer $\frac{1}{5}$ of dorso-ventral diameter of segment. Ventral canals very large, $\frac{2}{3}$ of dorso-ventral and $\frac{1}{8}$ to $\frac{1}{6}$ of lateral diameter of segment, connected distally in each segment by transverse canal 88μ in diameter; dorsal canals much smaller, $\frac{1}{14}$ of dorso-ventral and $\frac{1}{60}$ of transverse diameter of segment, situated dorso-median of ventral canals. Lateral nerve about half-way between ventral canal and lateral margin. Calcareous corpuscles absent. Maturity of segments attained about 35 mm. from anterior end of strobila. Genital pores unilateral in proximal third of margin. *Male* organs: Testicles, 35 to 44μ in diameter, 14 or 15 on each transverse section, arranged in single dorsal and ventral rows; vas deferens extends in convolutions about $\frac{1}{3}$ across the segment, dorsally of longitudinal canals and nerves; cirrus pouch pyriform, 79μ long by 49μ broad, does not quite reach the longitudinal nerve. *Female* organs: Ovary extends across the segment, from ventral canal to ventral canal; vitellogene gland nearly globular, median, dorsal of ovary, its transverse diameter about $\frac{1}{8}$ of the segment; vulva dorsal of cirrus; vagina extends dorsally of nerve and lateral canals, and at dorsal canal it widens into large, elongate, receptaculum seminis; uterus breaks up into 60 to 70 egg balls in each segment; mature eggs not observed, but probably about 38.6 by 36.4μ .

HABITAT.—Adult in intestine of man. Larval stage unknown, probably in some invertebrate.

GEOGRAPHIC DISTRIBUTION.—Known only for Aschabad, Asiatic Russia.

MEDICAL SIGNIFICANCE.—Unknown.

PREVENTION.—Unknown.

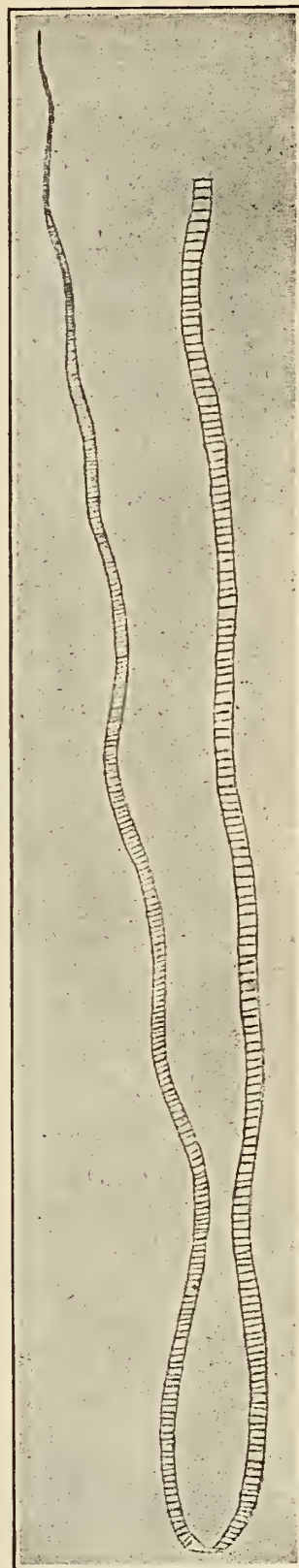


FIG. 109.—Strobila of *Davainea asiatica*. Natural size. (After Linstow, 1901, 983, fig. 1.)

^a SYNONYM.—*Tænia* [*Davainea*] *asiatica*, Linstow, 1901.

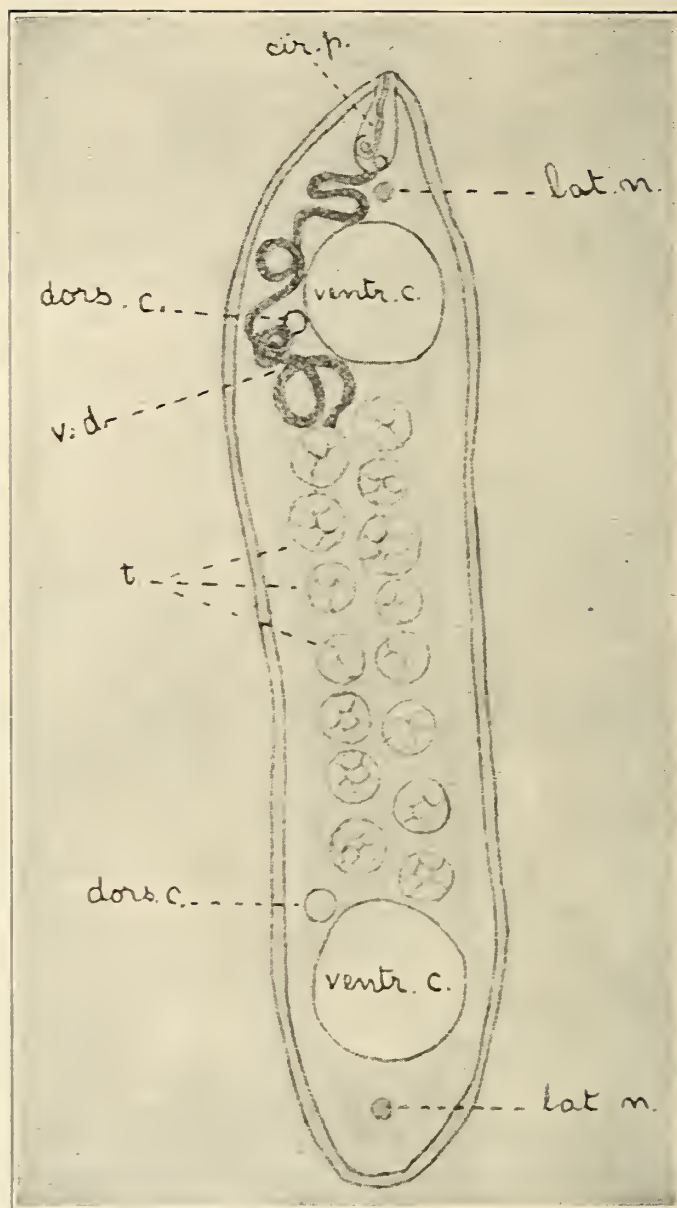


FIG. 110.—Diagram of transverse section of same to show the male organs: *cir. p.*, cirrus pouch; *dors. c.*, dorsal canals; *lat. n.*, nerves; *t.*, testicles; *ventr. c.*, ventral canals; *v. d.*, vas deferens. Enlarged. (After Linstow, 1901, 983, fig. 2.)

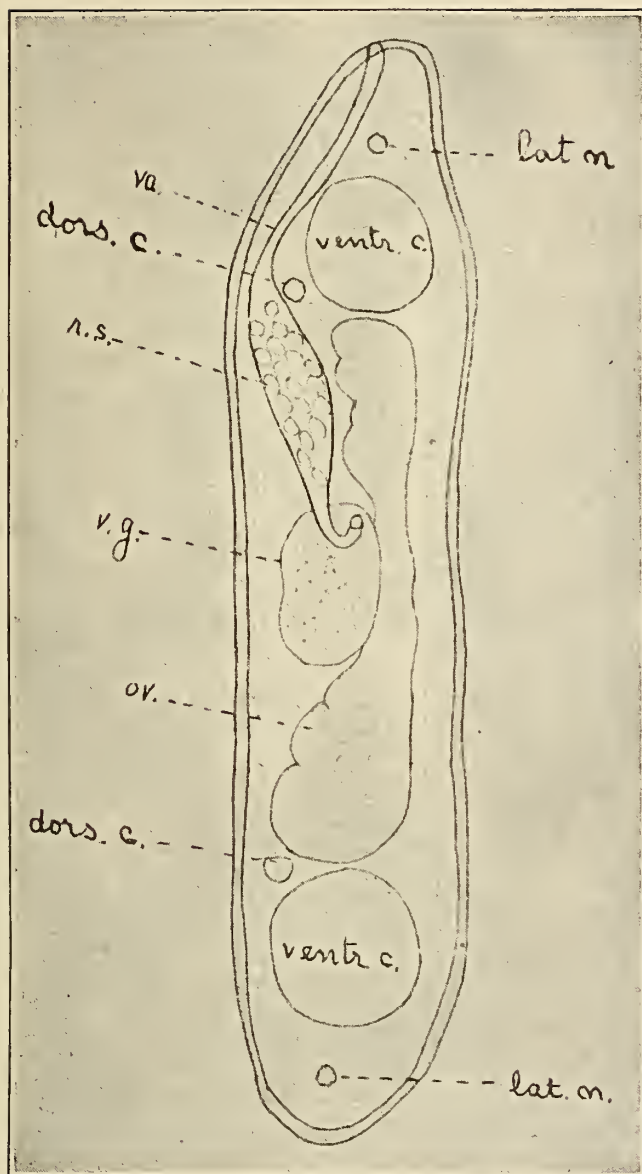


FIG. 111.—Diagram of transverse section of same to show the female organs: *ov.*, ovary; *r. s.*, receptaculum seminis; *va.*, vagina; *v. g.*, vitellogene gland; other letters same as in fig. 110. Enlarged. (After Linstow, 1901, 983, fig. 3.)

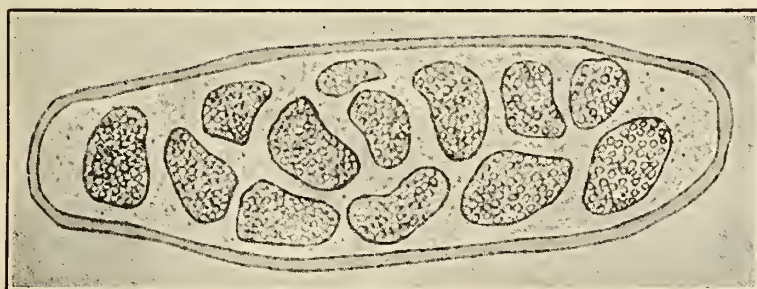


FIG. 112.—Transverse section of gravid segment to show the egg balls. Enlarged. (After Linstow, 1901, 984, fig. 4.)

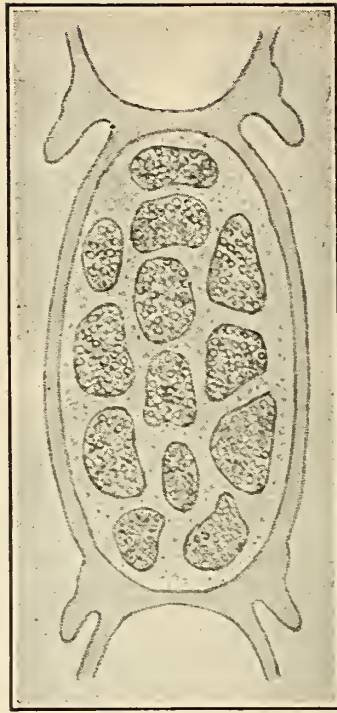


FIG. 113.—Sagittal section of same to show egg balls and the general outline of the segment. Enlarged. (After Linstow, 1901, 984, fig. 5.)

SOMATIC TÆNIASIS.

Somatic tæniasis is the infection of any organ with the larval stage of a tapeworm. In man we may have the four forms of somatic tæniasis mentioned on pp. 9–10.

Family TÆNIIDÆ.

(Subfamily TÆNIINÆ.)

CYSTICERCOSIS—INFECTION WITH CYSTICERCUS.

Infection with *CYSTICERCUS CELLULOSÆ*.^a

[Figs. 54, 114 to 119.]

SPECIFIC DIAGNOSIS. See p. 37.

On p. 39 attention was directed to the fact that *Tænia solium* is a more dangerous parasite than *T. saginata* because of the danger of autoinfection. If, for instance, a patient who harbors *T. solium* soils his fingers with his feces, containing the eggs, and through carelessness infects himself with these eggs *per os*, or if through a reverse peristalsis a gravid segment of the worm gains access to his stomach, the onchospheres (embryos) upon becoming free from their shell, bore through the intestinal wall and come to rest in the muscles, eye, brain, or elsewhere, and develop into the cysticercal stage. In case of infection with *Tænia saginata* this danger of autoinfection is not present.

^aSYNONYMS See p. 30.

The seriousness of the cysticercal infection depends upon the location of the parasites and the number present.

CLINICAL DIAGNOSIS.—In case of superficial infection, the parasites may sometimes be felt through the skin; in case of infection in the eye,

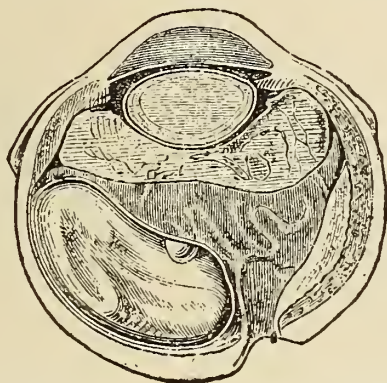


FIG. 114.—Subretinal cysticercus in the eye. $\times 1$. (After von Wecker; from Leuckart, 1880, 700, fig. 298.)

diagnosis is made by ophthalmoscopic examination; in case of cerebral infection, a presumptive diagnosis is made upon the clinical history combined with a positive knowledge of preexisting intestinal tæniasis due to *Tænia solium*.

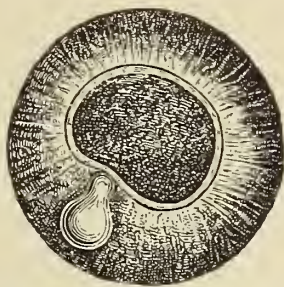


FIG. 115.—Cysticercus in anterior chamber. $\times 3$. (After von Wecker; from Leuckart, 1880, 701, fig. 299.)

TREATMENT.—No medicinal treatment established. The parasites may, in many cases, be removed surgically.

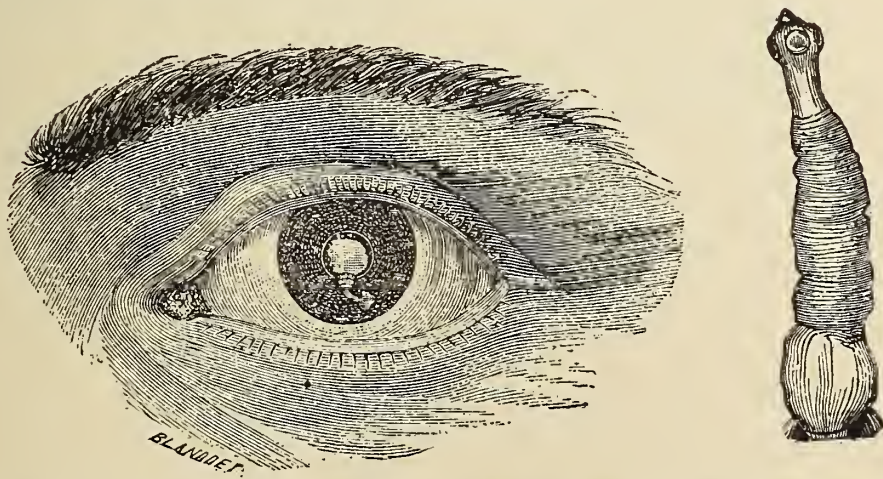


FIG. 116.—A cysticercus in the anterior chamber; A, isolated head. (After Blanchard, 1886a, 402, fig. 244.)

PREVENTION.—Great personal cleanliness on the part of patients harboring *Tænia solium*; such patients should not occupy a bed with other persons; prevention of *T. solium*, see p. 39.

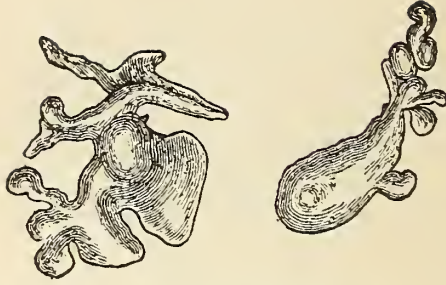


FIG. 117.—Racemose cysticerci. $\times 1$. (After Marchand, from Leuckart, 1880, 702, fig. 300.)

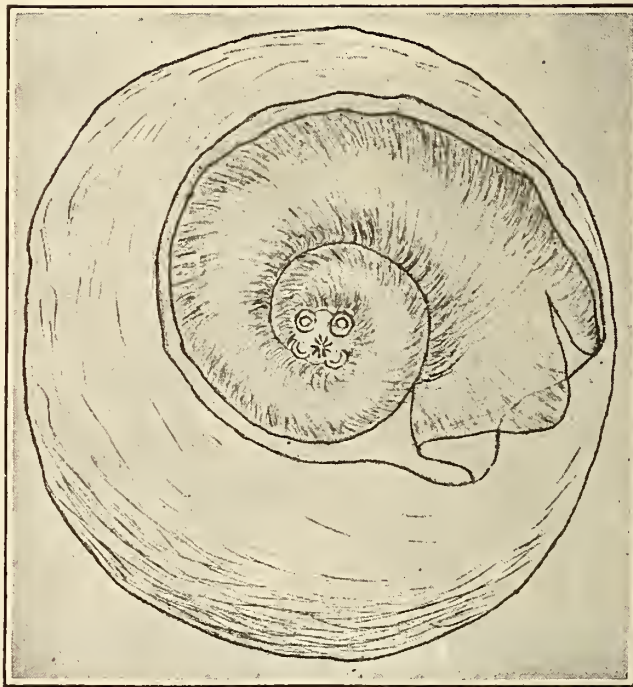


FIG. 118.—A cysticercus from the brain. $\times 12$. (After Leuckart, 1880, 702, fig. 301.)

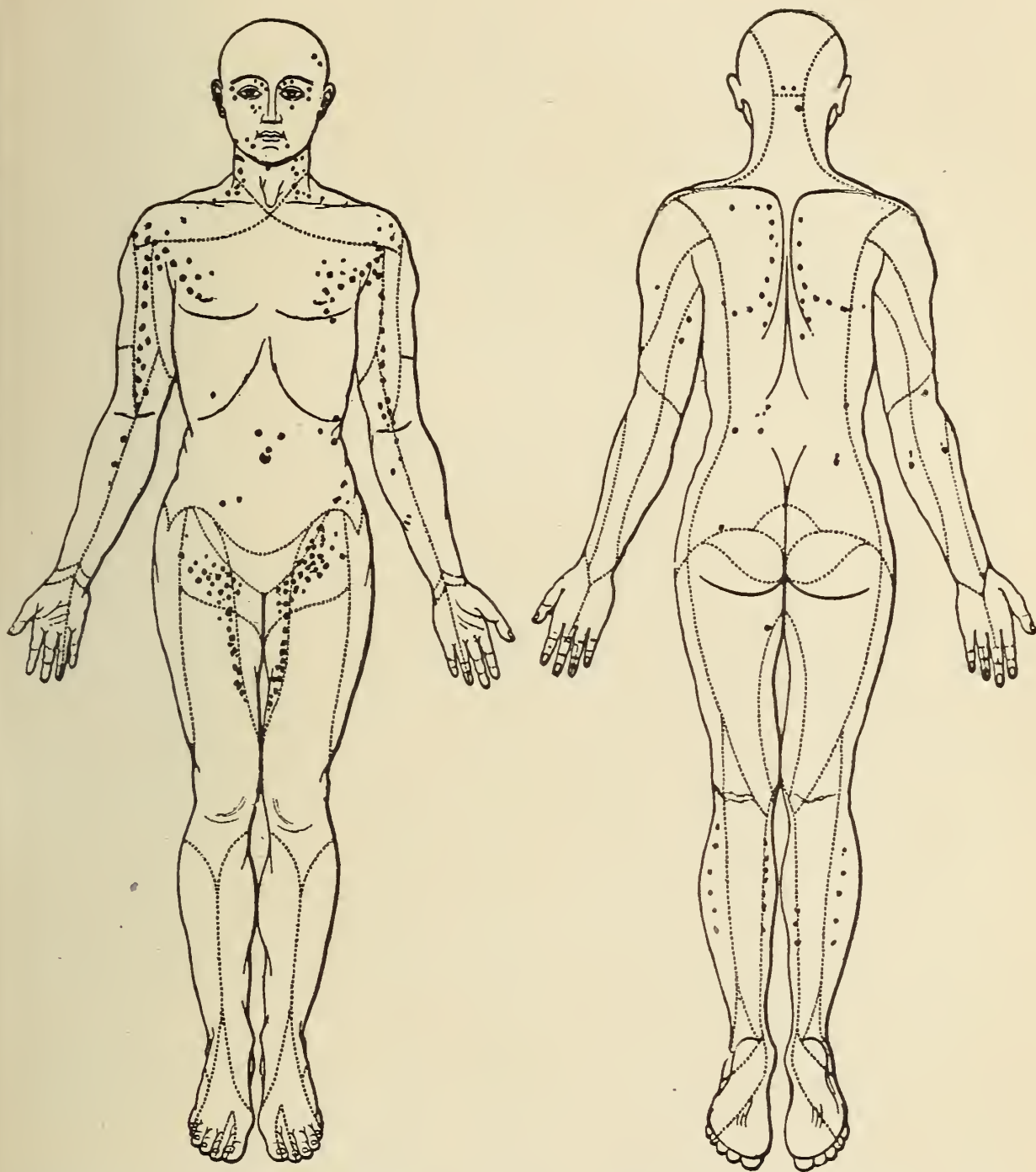


FIG. 119.—Symmetrical distribution of cysticerci in the subcutaneous connective tissue (After J. Loeb; from Huber, 1896a, 567, fig. 82.)

The so-called *CYSTICERCUS VISCERALIS* and *CYSTICERCUS TENUICOLLIS HOMINIS*.

Early authors record as parasitic in man a cystic worm, which has been classified by various writers as *Cysticercus tenuicollis*, the larval stage of *Tænia hydatigena* (see p. 72) of dogs. Such serious doubts arise, however, in regard to the correctness of the zoological determination, that these parasites,^a or alleged parasites, must at present be considered as unidentifiable. The parasite reported by Eschricht (1853a) as *Cysticercus tenuicollis* and quoted by Diesing (1864a) as *Cysticercus tenuicollis hominis* appears to have been a true *C. tenuicollis*; but, according to Krabbe (1866b), Eschricht has since stated that he believes this specimen came from sheep, instead of from man. Hodges (1867a, b) has reported a *Cysticercus tenuicollis* for man in the United States, but Braun (1894e) considers that this specimen may equally well be interpreted as a *C. cellulosæ*.

In view of the foregoing discussion, *Cysticercus tenuicollis* should not be definitely accepted as a parasite of man unless further and unequivocal cases are reported.

SPECIFIC DIAGNOSIS of *Tænia hydatigena*^b (figs. 120 to 123).—*Tænia* (*Tænia*) (p. 36): Strobila attains 1.5 to 5 mm. in length. Head reniform, about 1 mm. in diameter; rostellum long and narrow, armed with a double row of 30 to 44 hooks, alternating large (180 to 220 μ) and small (110 to 160 μ). Neck rather long, nearly as broad as head. Segments become square about 60 cm. from head; distal border of segment irregularly undulate and covering proximal border of next segment like a cuff. Genital pore slightly salient. Gravid segments 50 to 70 in number, 4 to 7 mm. broad by 10 to 14 mm. long. Uterus with 5 to 8 lateral branches each side. Embryophores nearly spherical, 31 to 36 μ in diameter.

Cysticercus stage (*C. tenuicollis*^c) attains considerable size, 16 cm. long by 6 to 7 cm. broad, or even larger (fig. 123).

^a*Tænia visceralis* Gmelin, 1790a; *Cysticercus visceralis* (Gmelin, 1790a) Zeder, 1803a; *Finna visceralis* Brera, 1809a; *Cysticercus visceralis hominis* Rudolphi, 1810a; "*C. visceralis treutleri* Slawikowski, 1819."

^bSYNONYMS.—*Tænia solium* Linnæus, 1758a in part; *T. cateniformis* Gœze, 1782a; ? *T. serrata* Gœze, 1782a, in part; *T. marginata* Batsch, 1786a; *T. lupina* Schrank, 1788; *T. cateniformis lupi* Gmelin, 1790a; *Halysis marginata* (Batsch, 1786a) Zeder, 1803a.

^cSYNONYMS.—*Lumbricus hydropicus* Tyson, 1691; *Vermes vesiculares* Hartmann, 1705b; *Tænia hydatoidea* Pallas, 1760; *T. hydatigena* Pallas, 1766; *Hydra hydatula* Linnæus, 1767; *Vermis vesicularis eremita* Bloch, 1780a; *Hydatigena orbicularis* Gœze, 1782a; *H. globosa* Batsch, 1786a; *H. oblonga* Batsch, 1786a; *Vesicaria orbicularis* (Gœze, 1782a) Schrank, 1788; *Tænia simiæ* Gmelin, 1790a; *T. ferarum* Gmelin, 1790a; *T. caprina* Gmelin, 1790a; *T. ovilla* Gmelin, 1790a; *T. vervecina* Gmelin, 1790a; *T. bovina* Gmelin, 1790a; *T. apri* Gmelin, 1790a; *T. globosa* (Batsch, 1786a) Gmelin, 1790a; ? *Hydatula lienis* Gmelin, 1790a; ? *H. pulmonis* Gmelin, 1790a; *H. hepatis* Gmelin, 1790a; *H. cervorum* Gmelin, 1790a; *H. peritonæi* Gmelin, 1790a; *H. solitaria* Viborg, 1790; *Cysticercus clavatus* Zeder, 1803a; *C. globosus* (Batsch, 1786a) Zeder, 1803a; *C. simiæ* (Gmelin, 1790a) Zeder, 1803a; *C. caprinus* (Gmelin, 1790a) Zeder, 1803a; *C. lineatus* Lænnec, 1804; *Physchiosoma globosum* (Batsch, 1786a) Brera, 1809a;

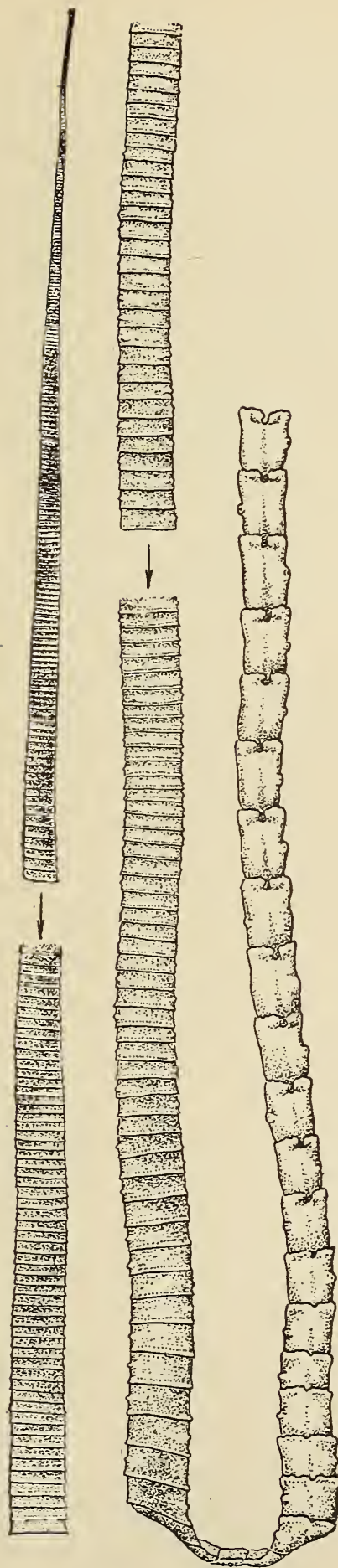


FIG. 120.—Strobila of *Tænia hydatigena* of the dog. Natural size. (After Stiles, 1898a, 97, fig. 85.)

Cysticercus tenuicollis Rudolphi, 1810a; *C. visceralis simiæ* Rudolphi, 1810a; *Tænia visceralis vesicularis orbicularis* Goeze of Lænnec, 1812; *T. hydatigena ovium* Pallas of Lænnec, 1812; *T. hydatigena suum* Pallas of Lænnec, 1812; *Hydatis globosa* (Batsch,

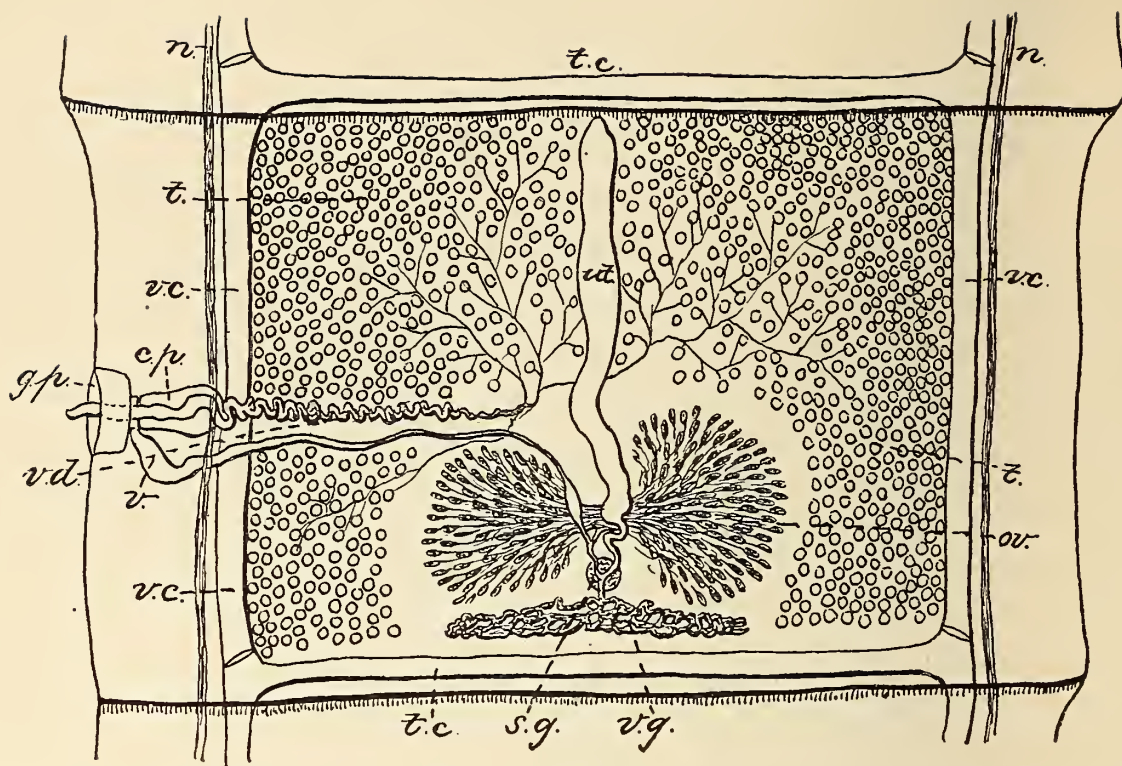
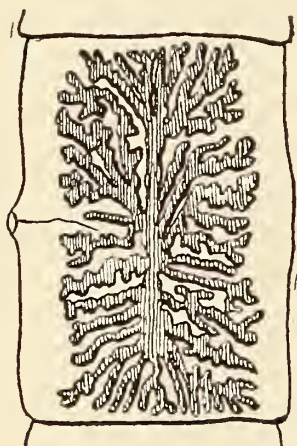
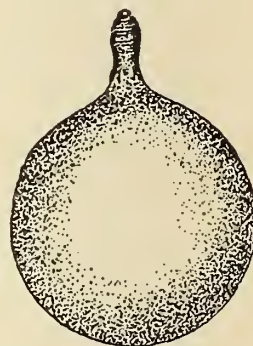


FIG. 121.—Mature segment of same, enlarged to show the anatomy: *c. p.*, cirrus pouch; *g. p.*, genital pore; *n.*, nerve; *ov.*, ovary; *s. g.*, shell gland; *t.*, testicles; *t. c.*, transverse canal; *ut.*, uterus; *v.*, vagina; *v. c.*, ventral canal; *v. d.*, vas deferens; *v. g.*, vitellogene gland. (After Deffke, 1891a; pl. 1, fig. 1.)

B.



122



123

FIG. 122.—Gravid segment of same, enlarged to show lateral branches of uterus. (After Leuckart, 1880, 720, fig. 308b.)

FIG. 123.—*Cysticercus tenuicollis* from a steer. Natural size. (After Stiles, 1898a, 97, fig. 84.)

HABITAT.—Adults in intestine of canines, as dogs and wolves; cysticercus in body cavity of various domesticated animals, as cattle, sheep, goats, swine; also reported for a number of wild animals.

GEOGRAPHIC DISTRIBUTION.—More or less cosmopolitan.

1786a) Lamarck, 1816; *Fischiosoma globosum* Brera of delle Chiaje, 1825a; *Tænia ferrarum* Gmelin of Diesing, 1850a; *Cysticercus hominis dubius* Diesing, 1854b; *C. ex potamochæro penicillato* Cobbold, 1861d; *C. potamochæri penicillati* Cobbold, 1861e; *C. potamochæri* Cobbold, 1861e; *C. tenuicollis hominis* Eschricht of Diesing, 1864a; *C. ovis* Cobbold, 1869a; *C. ovipariens* Maddox, 1873; *C. phacochæri æthiopici* Cobbold of Linston, 1878; *Cisticercus ovis* (Cobbold, 1869) Guzzardi Asmundo, 1885a.

This is the parasite which has been reported as *Tænia solium* of the dog by several authors, and by at least one State Board of Health.

Unidentifiable Cysticeri (?).

In the foregoing discussion certain parasites have been cited in the tables of synonymy, although I consider them at present unidentifiable; still, other authors have claimed to have recognized them as identical with the species in connection with which they have here been given, and not being able to disprove the synonymy, I have accepted the views of these authors.

There still remain certain parasites which I have not been able to classify, namely:

"*Cysticercus aortæ* Notarjanni" is quoted by Tschudi, 1837, 53, as synonym of *Cysticercus cellulosæ*; and "*Cysticercus aorticus* Notar," is mentioned by Moquin-Tandon, 1860, 369, but I have been unable to find the original description; Moquin-Tandon says that the body is oval and provided with filiform hooks.

Cysticercus hepaticus Brera is mentioned by Tschudi, 1837, 53, as a synonym of *Cysticercus cellulosæ*; and Moquin-Tandon, 1860, 369, mentions a *Cysticercus hepaticus* delle Chiaje, with *Trichosoma hepaticus* Brera as synonym. I have been unable to trace these names, unless reference is made to *Finna hepatica* Brera, 1809a, 159; 1810a, pl. 3, fig. 4.

HYDATID DISEASE—ECHINOCOCCOSIS.

[FIGS. 124 to 136.]

Hydatid disease or echinococcosis is the infection of any organ with the cystic stage of a very small tapeworm which lives in canines.

Genus ECHINOCOCCUS^a Rudolphi, 1801.

GENERIC DIAGNOSIS.—*Tæniinæ* (see p. 23): Strobila small (type species less than 7 mm. long), and composed of few segments (type species not over 4 or 5), of which only the terminal (posterior) segment is gravid. Head armed with double row of hooks. Genital pores marginal, irregularly alternate. Cystic stage an *echinococcus*, with or without daughter cysts; several scolices develop in each of the numerous brood capsules. Adults in carnivorous animals, cystic stage in herbivorous and omnivorous mammals.

TYPE SPECIES.—*Echinococcus granulosus* in sheep and calves.

^aSYNONYMS.—*Hydatis* Gœze, 1782a (doubtful whether this is used in a generic sense); *Echinococcus* Rudolphi, 1801; *Acephalocystis* Lænnec, 1804 and 1812; *Liococcus* Bremser, 1819a; *Splanchnococcus* Bremser, 1819a; *Acephalocystus* Lænnec of Merat, 1821; *Acephalocistis* Cruveilhier, 1829a; ?? *Acrostoma* Lesauvage, 1829; ? *Astoma* Goodsir, 1844d; ? *Diskostoma* Goodsir, 1844; ? *Sphæridion* Goodsir, 1844 (?); *Echinococcifer* Weinland, 1858; *Ecchinococcus* Lœbel, 1870a; ? *Discostoma* Braun, 1894a; *Echinokokkus* of various German authors.

The Hydatid Tapeworm—*ECHINOCOCCUS GRANULOSUS*^a (Batsch, 1786)
Rudolphi, 1805.

[Figs. 124 to 131.]

SPECIFIC DIAGNOSIS.—*Echinococcus* (p. 75): Strobila very small, 2.5 to 5 mm., exceptionally 6.5 mm. long. Head very small, subglobular, scarcely 0.3 mm. in diameter; rostellum prominent, armed with a double row of 28 to 50 hooklets, the large hooks 22 to 30 μ (40 to 45 μ Leuckart), the small hooks 18 to 22 μ (30 to 38 μ Leuckart); suckers 0.13 mm. in diameter; neck continues insensibly into the first portion of the strobila, which is devoid of segmentation. This is followed by the first segment, which is about as broad as long and is sterile. The second segment may be twice as broad and four times as long as the preceding and contains male and female organs. The third (terminal) segment is gravid; it may attain 2 mm. in length by 0.6 mm. in breadth, and contains about 500 eggs. Calcareous corpuscles present. Male organs: Cirrus pouch large, 0.5 mm. reaching nearly to median line of segment; testicles 70 μ in diameter, about 60 to the segment. Female organs: Vagina with large, elongate, setose dilatation 0.05 mm. in diameter; vagina continues caudad into a dilated 0.014 mm. receptaculum seminis; ovaries 2, lobate, submedian, about halfway between genital pore and distal end of segment; vitellogene gland sacular, near distal end of segment; uterus rather late in developing; "shell-gland" apparently absent. Embryophores 32 to 36 μ by 25 to 30 μ . Habitat, small intestine of carnivorous animals (*Canis*).

Cystic stage may attain the size of a fist or even of a babe's head, but is of slow growth, with thick external lamellated cuticle and thin internal parenchymatic layer; pedunculate brood capsules form from the latter, and in each of these several scolices form. Daughter cysts may also form. Habitat, various organs of herbivorous and omnivorous mammals.

Hosts.—*Of strobila*: Domesticated dog (*Canis familiaris*), wolf (*C. lupus*), jackal (*C. aureus*), dingo^b (*C. dingo*), cats (*Felis catus domestica*), and probably cougar (*F. concolor*).

Of cystic stage: Not infrequent in man (*Homo sapiens*); more common in the domesticated food-animals, cattle (*Bos taurus*), sheep (*Ovis aries*), goats (*Capra hircus*), swine (*Sus scrofa domestica*); also reported for crab-eating macaque (*Macacus cynomolgus*), Indian lion-tailed macaque (*M. silenus*), Barbary macaque (*Inuus inuus*), the argali (*Ovis ammon*), bactrian camel (*Camelus bactrianus*), dromedary (*C. dromedarius*), giraffe (*Giraffa camelopardalis*), wild boar (*Sus scrofa*), four-horned antelope (*Tetraceros quadricornis*), European elk or moose (*Alce alces*), zebra (*Equus zebra*), horse (*E. caballus*), ass (*E. asinus*), Malayan tapir (*Tapirus indicus*), domesticated dog (*Canis familiaris*), leopard (*Felis pardus*), domesticated cat (*F. catus domestica*), ichneumon (*Herpestes ichneumon*), common European squirrel (*Sciurus vulgaris*), kangaroo (*Macropus major*).

^a Synonyms of strobila stage.—*Tænia cateniformis* of Rudolphi, 1808a, 411, misdetermined; *T. cucumerina* Bloch of Diesing, 1850a, in part; *T. serrata* [young] of Roell, 1852, misdetermined; *T. echinococcus* Siebold, 1853; *T. serrata juvenalis röllii* Kuechenmeister, 1853; *Echinococcifer* Weinland, 1858 (type *T. echinococcus*); *Tenia nana* van Beneden, 1861a; *Echinococcifer echinococcus* (Siebold, 1853) Weinland, 1861; *Tænia echinococca* of Kœberlé, 1861a; *T. [(Echinococcifer)] echinococcus* of Leuckart, 1863; *T. (Arhynchotænia) echinococcus* of Diesing, 1864a; *T. nana* (Beneden, 1861) Diesing, 1864a [not Siebold, 1852]; *T. serrata röllii* Kuechenmeister of Diesing, 1864a; *T. echinoccus* Linstow, 1878; *T. [(Echinococcus)] echinococcus* of Railliet, 1886.

For synonymy of cystic stage see foot notes pp. 77–82.

^b The form from the dingo is said to attain 10 to 30 mm. in length. If these measurements are correct, this form doubtless represents a new species.

SPECIAL MEDICAL SIGNIFICANCE.—The cystic stage of *echinococcus* is found in practically every organ of the human body, but especially in the liver, lungs, and kidneys. It is more common in females than in males, and more common between the ages of 21 and 40 years.

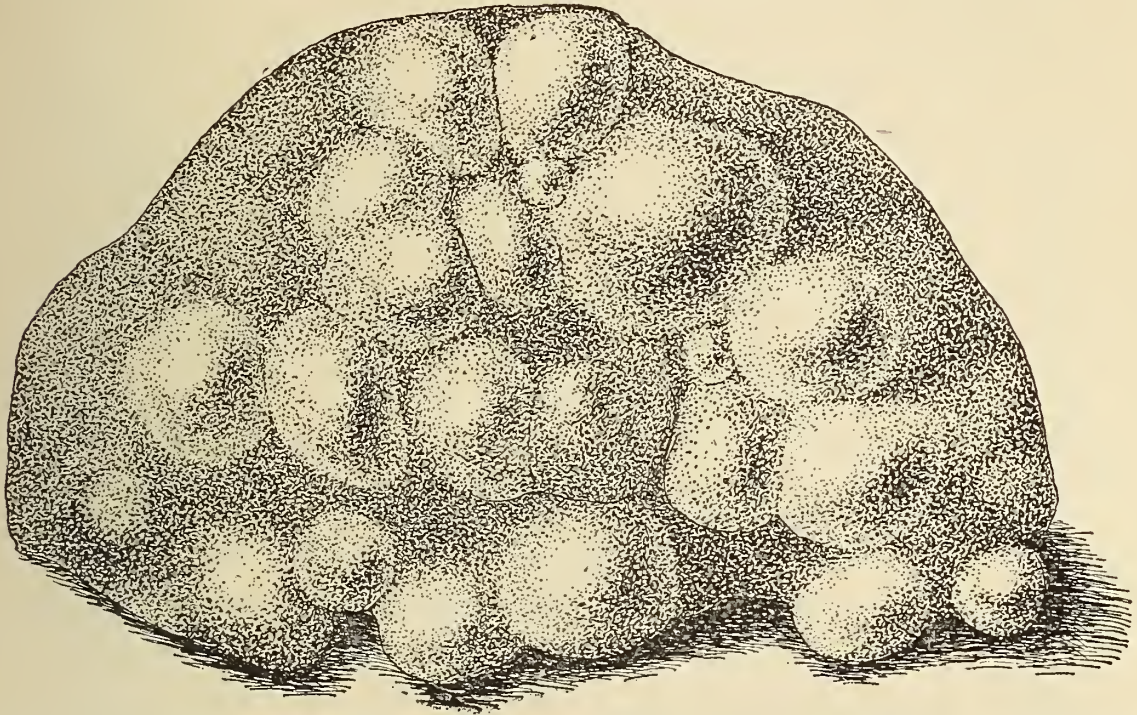


FIG. 124.—Portion of hog's liver infested with *echinococcus hydatid*. Natural size. (After Stiles, 1898a, 112, fig. 101.)

The symptoms are practically those of pressure from a slowly growing mass. Treatment is surgical.

PREVENTION.—Keep dogs away from slaughterhouses, thus preventing them from becoming infected with the tapeworm by ingestion of the cystic stage found in food animals; avoid undue intimacy with dogs, thus preventing infection from dogs by infection through contamination with the eggs; destroy ownerless dogs.

MODIFICATIONS IN FORM.—The cystic stage of *Echinococcus* assumes various modifications, to which different names have been given, either by intentional renaming of forms already known or under the assumption that the forms in question represented distinct species. Several names^a have been proposed as general designations to include all of these modifications.

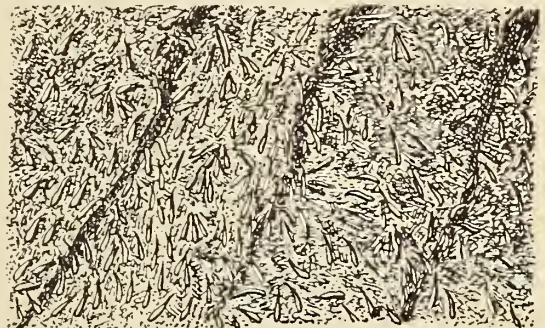


FIG. 125.—Portion of the intestine of a dog infested with the adult Hydatid Tapeworm (*Echinococcus granulosus*). Natural size. (After Ostertag, 1895, 430, fig. 99.)

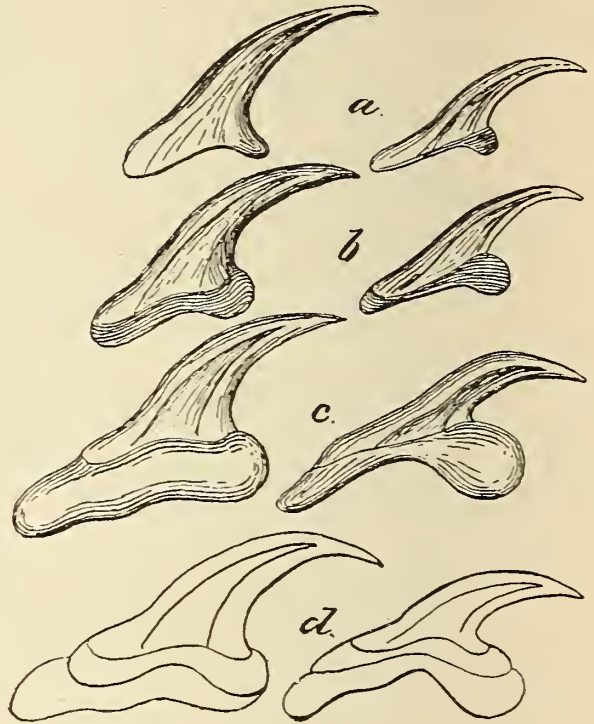
^a General names, including several or all modifications: *Echinococcus infusorium* Leuckart, 1827; *Polycephalus volvox* Tschudi, 1837; *P. echinococcus* Tschudi, 1837; ?*E. variabilis* Siebold, 1837, not accessible (see *E. variabilis* Huxley, 1852); *E. polymorphus* Diesing, 1850a; *E. cysticus* Huber, 1891b; *E. unilocularis* Huber, 1896a.

Several other names^a have been based upon the names of the hosts in which the parasites occur, thus intimating that they are viewed as distinct or probably distinct species.

A number of names^b have been based upon the organs in which the parasites occur.



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FIG. 126.—Adult Hydatid Tapeworm (*Echinococcus granulosus*). Enlarged. (After Leuckart, 1880, 743, fig. 316.)

FIG. 127.—Hooks of Hydatid Tapeworm: *a*, from a hydatid; *b*, three weeks after feeding to a dog; *c*, from an adult; *d*, combined figures of *a-c*, showing the gradual changes in form. $\times 600$. (After Leuckart, 1880, 736, fig. 315.)

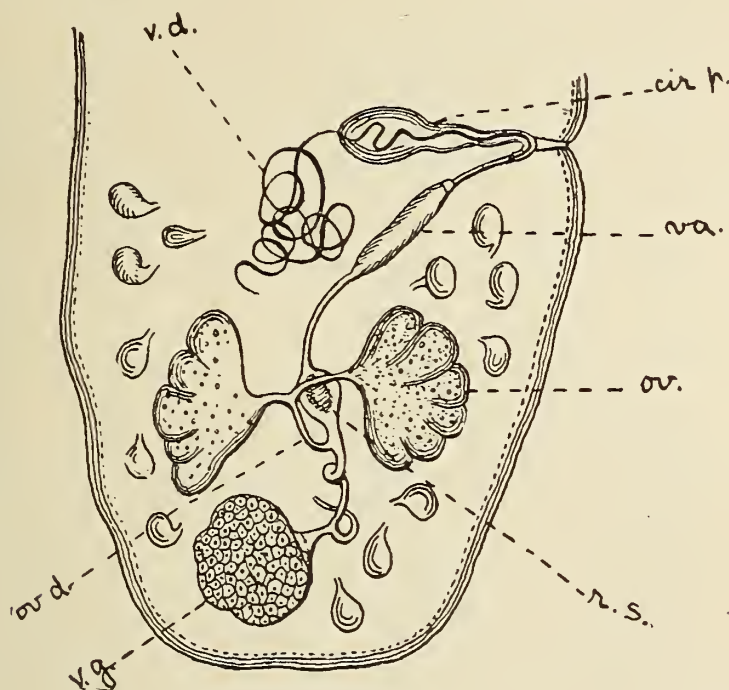
Quite a large number of names have been based upon modifications in growth, but to understand these we must consider the method of development.

When the six-hooked embryo (onchosphere) comes to rest in an organ, it gradually increases in size. After a time it consists of a thick

^a Names based upon the names of hosts: *Polycephalus hominis* Zeder, 1800a; *P. humanus* Zeder, 1803a; *Acephalocystis humana* Luederssen, 1808; *A. suilla* Luederssen, 1808; *Echinococcus hominis* (Zeder, 1800) Rudolphi, 1810a; *E. simiæ* Rudolphi, 1810a (*Hydatis erratica* Blumenbach, 1805, renamed); *E. simiæ cynomolgi* Oken, 1815; *E. suis* author? date?; *E. giraffæ* Gervais, 1847a; *E. arietis* E. Blanchard, 1848; *E. giraffæ* Diesing, 1850a; *E. pardi* Huxley, 1852?; "*Acephalocystis macaci*?" Cobbold, 1861e; ? *Acephalocystis ovis tragelaphi* Cobbold, 1861e.

^b Names based upon organs in which the parasites occur: *Echinococcus cerebri* Spiering, 1862; *E. hepatis* Scholler, 1862, and Kehlberg, 1873; *E. process. vermiformis* Scholler, 1862; *E. lienis* Ber. Krankenanst. Rudolf-Stiftung, Wien, 1867, and Kehlberg, 1873; *E. pulmonum*. Huppert, 1875a; *E. intracranialis* Fricke, 1880a (*E. intercranialis* of Stiles, 1896, misprint); *E. retroperitonealis* Bitter, 1886a (*E. retroperitonialis* of Stiles, misprint); *E. mesenterii* Surmann, 1891; *E. subdiaphragmalis-præperitonealis* Krasnoff, 1895a; *E. cerebri* Perroncito, date? (probably based on "*Echinococchi cerebri*" Perroncito, 1882, p. 172); *E. subphrenicus* Huber, 1896a.

external lamellated cuticle and an inner parenchymatic layer surrounding a lumen containing a fluid. This is the stage described as the *Acephalocystis*,^a the name being based upon the absence or the supposed absence of heads. As a matter of fact, the so-called acephalocysts probably contained heads in not a few cases, but as these scolices are small they might have been overlooked. Not all so-called acephalocysts are true echinococci.



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FIG. 128.—Sexual organs of adult tapeworm, *Echinococcus granulosus*: *cir. p.*, cirrus pouch; *ov.*, ovary; *ov. d.*, oviduct; *r. s.*, receptaculum seminis; *va.*, vagina; *v. d.*, vas deferens; *v. g.*, vitellogene gland. Enlarged. (After Leuckart, 1886, 747, fig. 318.)

The brood-capsules may form directly on the parenchymatic layer, thus giving a granular appearance to the parasite, and this is evidently the explanation of the use of the name *granulosus* by several authors.

In other cases daughter cysts form and are found floating in the fluid of the mother cysts; granddaughter cysts may form in the daughter cyst; brood capsules may form in the mother cyst, the daughter cysts, and the granddaughter cysts. This variation with endogenous

^aNames based on the acephalocyst: *Acephalocystis* Lænnec, 1804; *A. humana* Luedersen, 1808; *A. suilla* Luedersen, 1808; *A. ovoidea* Lænnec, 1812; *A. cystifera* Lænnec, 1812; *A. ansa* Lænnec, 1812; *A. intersecta* Lænnec, 1812; *A. surculigera* Lænnec, 1812; *A. granosa* Lænnec, 1812; [*A. plana* Lænnec, 1812 = *Ovuligera carpi* Dupuytren, is not an echinococcus]; *Acephalocystus communis* Merat, 1821; *Acephalocystis communis* Lænnec, 1825; *A. eremita* Cruveilhier, 1829a; *A. sterilis* Cruveilhier, 1829a; *A. socialis* Cruveilhier, 1829a; *A. prolifera* Cruveilhier, 1829a; *Acephalocistis socialis* Cruveilhier, 1829a; *A. prolifera* Cruveilhier, 1829a; *Acephalocystis endogena* Kuhn, 1830 and 1832 (*A. socialis* vel *prolifera* renamed); *A. exogena* Kuhn, 1830 and 1832 (*A. eremita* vel *sterilis* renamed); *A. granulosa* delle Chiaje, 1833 (for *A. granosa* Lænnec); *A. prolifera socialis* Cruveilhier of delle Chiaje, 1833a; *A. eremita sterilis* Cruveilhier of delle Chiaje, 1833a; *A. simplex* Goodsir, 1844d; "*A. macaci*?" Cobbold, 1861e; ? *A. ovis tragelaphi* Cobbold, 1861e.

formation of secondary cysts is reported especially for man, and has been described under several different names.^a

In another variation in growth, found particularly in ruminants, the daughter cysts escape externally from the mother cysts. This is referred to as an exogenous formation; that daughter cysts may form

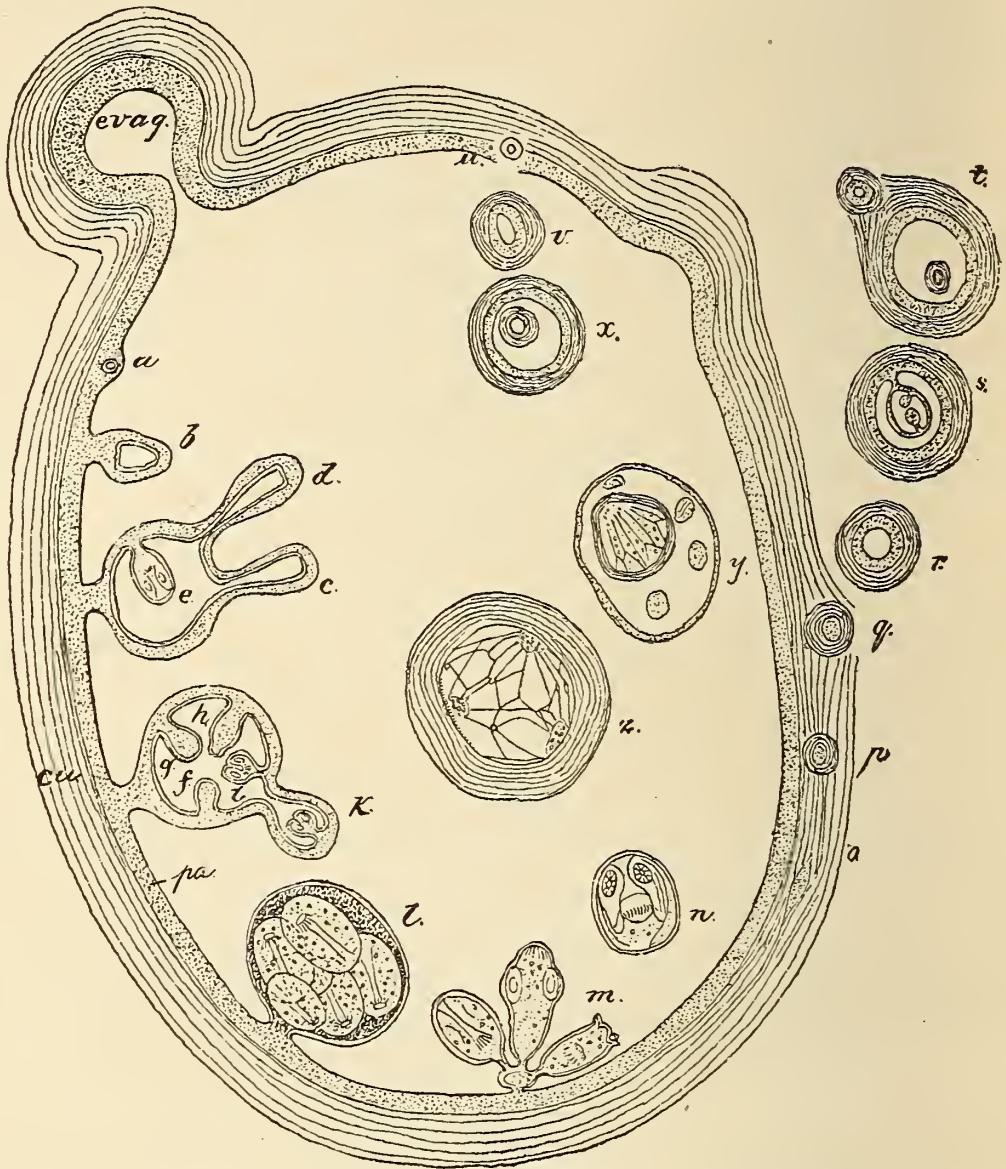


FIG. 129.—Diagram of an *Echinococcus* hydatid: *cu*, thick external cuticle; *pa*, parenchym (germinal) layer; *c*, *d*, *e*, development of the heads according to Leuckart; *f*, *g*, *h*, *i*, *k*, development of the heads according to Moniez; *l*, fully developed brood capsule with heads; *m*, the brood capsule has ruptured, and the heads hang in the lumen of the hydatid; *n*, liberated head floating in the hydatid; *o*, *p*, *q*, *r*, *s*, mode of formation of secondary exogenous daughter cyst; *t*, daughter cyst with one endogenous and one exogenous granddaughter cyst; *u*, *v*, *x*, formation of exogenous cyst, after Kuhn and Davaine; *y*, *z*, formation of endogenous daughter cysts, after Naunyn and Leuckart; *y*, at the expense of a head; *z*, from a brood capsule; *evag.*, constricted portion of the mother cyst. (After R. Blanchard, 1886a, 426, fig. 257, slightly modified.)

^aNames applied especially to the variation found more commonly in man, usually with endogenous formation of secondary cysts: *Polycephalus hominis* Zeder, 1800a; *P. humanus* Zeder, 1803a; *P. echinococcus* Zeder, 1803a; *Echinococcus hominis* (Zeder, 1800) Rudolphi, 1810a; *Liococcus* Bremser, 1819a; *Splanchnococcus laevis* Bremser, 1819a; *Echinococcus altricipariens* Kuechenmeister, 1855a; *Cysticercus echinococcus* (Zeder, 1803) Kœberlé, 1861a; *Echinococcus hydatidosus* Leuckart, 1863; *E. endogena* (Kuhn, 1830) Leuckart, 1863.

in all cases does not appear to have been demonstrated, but the cysts in animals have given rise to a number of additional names.^a

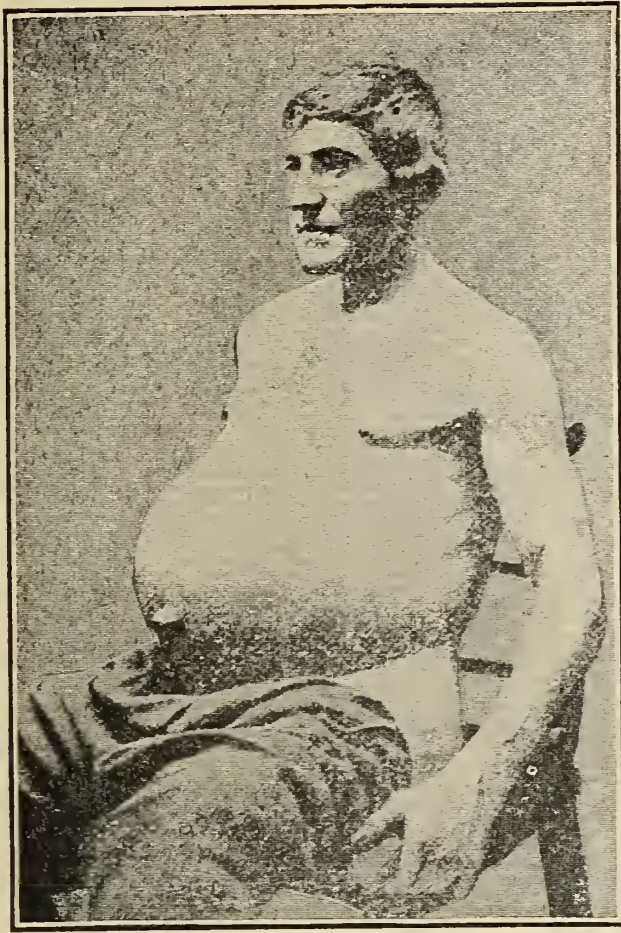


FIG. 130.—Echinococcus cyst in the liver of a man 50 years old. (After Huber, 1896a, 523, fig. 73.)

^aNames introduced especially for the cystic stage as it occurs in domesticated animals, and in many instances associated with exogenous daughter cysts: *Tænia visceralis socialis granulosa* Gøze, 1782a (from sheep and calves); *Hydatigena granulosa* Batsch, 1786a; *Vesicaria granulosa* (Batsch, 1786) Schrank, 1788; *Tænia visceralis granulosa* Gøze of Schrank, 1788; *T. granulosa* (Batsch, 1786) Gmelin, 1790a; *Polycephalus granulosus* (Batsch, 1786) Zeder, 1803a; *Echinococcus granulosus* (Batsch, 1786) Rudolphi, 1805, and Leuckart, 1863; *Tænia hydatigena granulosa* Rudolphi, 1805; *Echinococcus veterinorum* Rudolphi, 1810a (*Hydatigena granulosa* Batsch, 1786, renamed); *Polycephalus granosus* Lænnec, 1812; *Tænia granosa* Gmelin of Lænnec, 1812; *T. visceralis socialis granosa* Gøze of Lænnec, 1812; *Splanchnococcus echinatus* Bremser, 1819a; *Tenia visceralis socialis granulosa* Gøze of Diesing, 1850a; *Echinococcus scoleicipariens* Kuechenmeister, 1855a (*E. veterinorum* Rudolphi, 1810, renamed); *E. cænuroides* Kuechenmeister, 1855a (*E. veterinorum* Rudolphi, 1810, renamed); *Tænia echinococcus scoleicipariens* Kuechenmeister, 1855a; *Echinococcus simplex* Leuckart, 1886 (*E. scoleicipariens* Kuechenmeister, 1855, renamed); *E. exogena* (Kuhn, 1830) Blanchard, 1886a; *E. scolicipariens* Kuechenmeister of Stiles, 1898a, misprint.

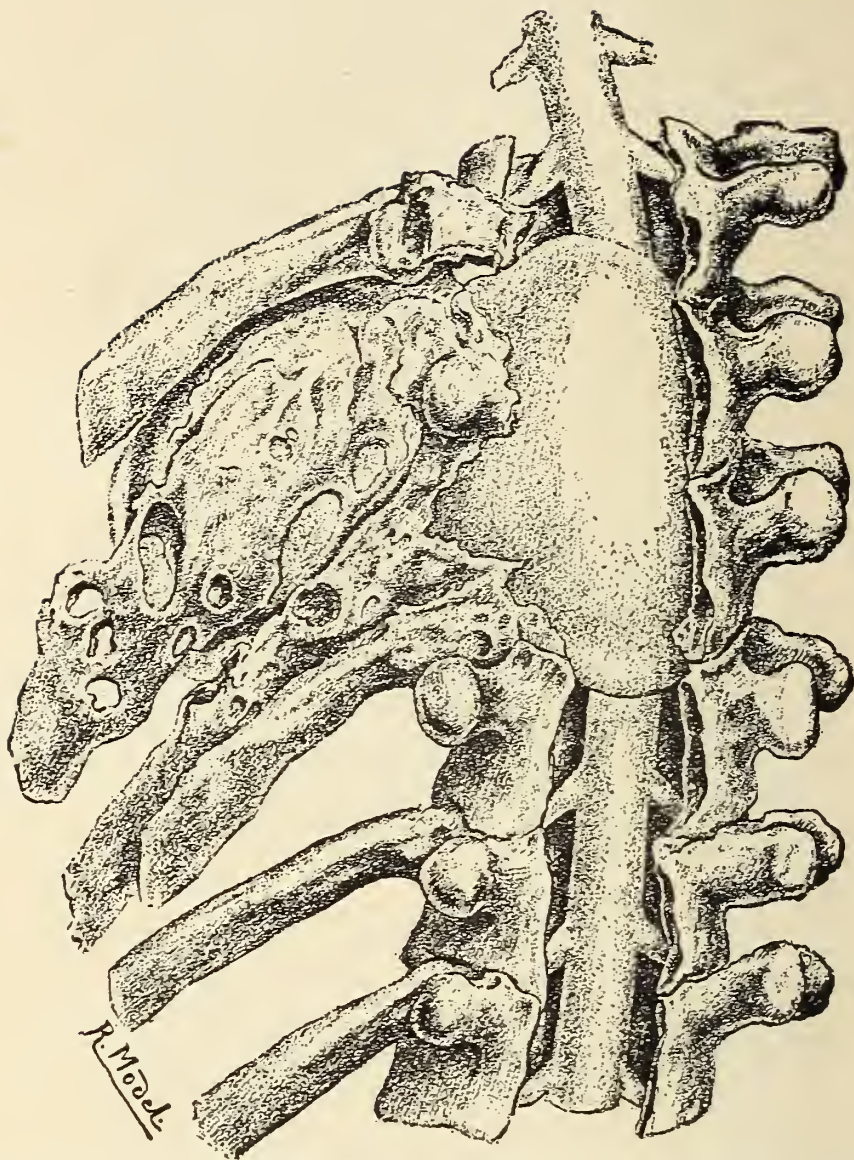


FIG. 131.—Echinococcus cyst of the spinal canal. (After Bellencontre; from Huber, 1896a, 550, fig. 76.)

Still other names^a have been proposed by various authors under various other circumstances.

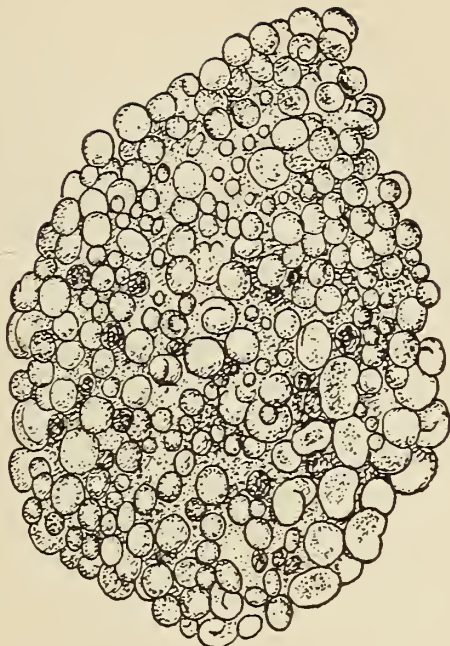
^aMiscellaneous names: *Hydatides singulares* Pallas, 1766, refers to echinococcus cysts in man and animals; *Hydatid erraticum* Blumenbach, 1805a, renamed *E. simiæ* Rudolphi, 1810a; *Finna idatoides* Brera, 1810a, in man; *Hydatid simplex* Home is quoted by delle Chiaje, 1833a, in connection with *Acephalocystis eremita sterilis*; ? *Astoma acephalocystis* Goodsir, 1844a; ? *Diskostoma acephalocystis* Goodsir, 1844a; *Echinococcus variabilis* Huxley, 1852a; *E. unilocularis* Hafiter, 1875a, apparently as distinction from *E. multilocularis*; *E. multiplex* Stiller, 1882.



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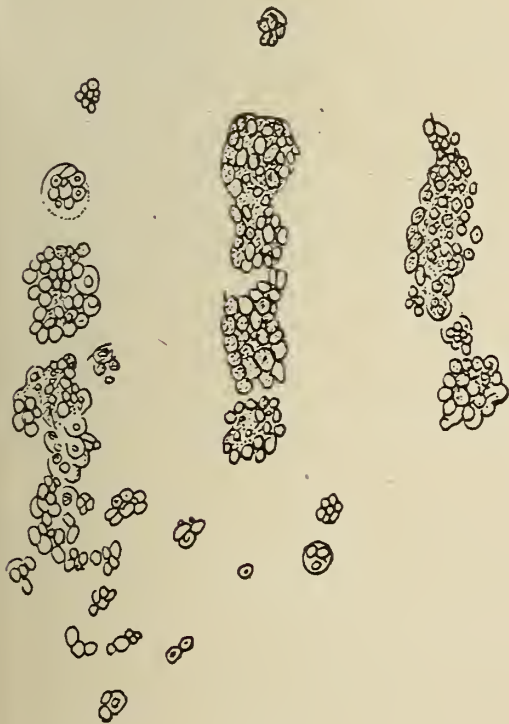


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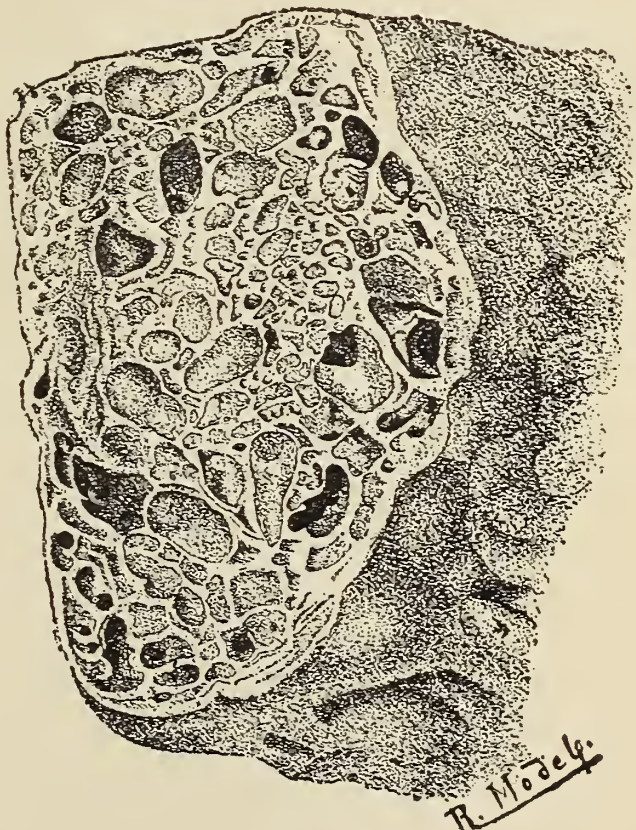
FIG. 132.—A racemose Echinococcus. Natural size. (After Leuckart, 1880, 795, fig. 334.)

FIG. 133.—Section through a multilocular Echinococcus. $\times 30$. (After Leuckart, 1880, 796, fig. 335.)

FIG. 134.—A multilocular Echinococcus from the liver of a steer. Natural size. (After Ostertag, 1895, 427, fig. 94.)



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FIG. 135.—A multilocular Echinococcus from the pleura of a hog. Natural size. (After Ostertag, 1895, 428, fig. 97.)

FIG. 136.—A multilocular Echinococcus. (After Luschka; from Huber, 1896a, 510, fig. 72.)

The Multilocular Echinococcus—**ECHINOCOCCUS GRANULOSUS MULTILOCULARIS**^a (Leuckart, 1863) Stiles, 1905.

[Figs. 132 to 136.]

A peculiar form of echinococcus cyst occurs in man and animals in certain localities, especially in Russia, Bavaria, Switzerland, Austrian Alps, and Wuerttemberg. Opinion differs as to whether it represents a distinct species or simply a modification of the ordinary form. It is here recognized as a subspecies.

SUBSPECIFIC DIAGNOSIS.—*Echinococcus granulosus* (p. 76): Strobila similar to that of the type form; some slight differences are reported, but these require further study and confirmation.

Cystic stage attains the size of a fist or even of a child's head, and represents a mass of numerous small cysts, 0.1 to 5 mm. in diameter; these cysts may communicate, according to some authors, or the cuticular layers are connected; brood capsules may be present; some of the cysts contain 1 to several heads, others are without scolices. This parasite is especially likely to undergo degeneration and represents the alveolarcolloid of certain authors.

HABITAT.—Cystic stage, especially in liver, but also in brain, spleen, suprarenal capsules, and secondarily through metastasis in various abdominal organs, also in lungs, heart, etc., of man, cattle, sheep, and swine. Adult strobila in dogs.

SPECIAL MEDICAL SIGNIFICANCE.—The nature of this parasitic growth was long misunderstood. Zenker has shown that the parasites are located in the lymphatic vessels; but they show a pronounced tendency to grow into other channels, especially into the bile ducts. They cause a very serious condition which, in man, nearly always results fatally.

PREVENTION.—Same as for the ordinary echinococcus, see p. 77.

Family **DIBOTHRIOCEPHALIDÆ**.

Collective Group **SPARGANUM** Diesing, 1855.

GENERIC DIAGNOSIS.—*Dibothriocephalidæ*: (p. 14) An artificial collective group to contain larval stages of bothriocephalid worms, which have not reached a stage in their development that they can be determined generically.

Such groups do not require a type species.

In man are found two immature parasites, which may be classified here. They are distinguished as follows:

KEY TO THE SPECIES OF SPARGANUM FOUND IN MAN.

- Worms attain 8 to 36 cm. in length and do not reproduce by fission or by the formation of supernumerary heads; Asia, ?Egypt, and South America.....
*Sparganum mansoni* (p. 85).
 Worms attain 1 to 12 mm. in length and may reproduce by fission and by the formation of supernumerary heads; Japan*S. proliferum* (p. 86).

^a **SYNONYMS.**—Die multiloculäre, ulcerirende Echinokokkengeschwulst Virchow, 1856; *Echinococcus multilocularis* Leuckart, 1863; Tumeur hydatique alvéolaire Carrière, 1868a; *Echinococcus multilocularis hepatis* Haffter, 1875a; *E. alveolaris* Klemm, 1883a, and Blanchard, 1886a; ?*E. racemosus* Leuckart, 1886; *E. multilocularis exulcerans* Huber, 1896a; *E. osteoklastes* Huber, 1896a; *Tania echinococcus alveolaris* (Klemm, 1883) Devé, 1905.

Manson's Larval Tapeworm—*SPARGANUM MANSONI*^a (Cobbold, 1882)
Stiles & Tayler, 1902.

[Figs. 137 to 143.]

SPECIFIC DIAGNOSIS.—*Sparganum*: Length, 8 to 36 cm.; breadth, 0.1 to 12 mm.; thickness, 0.5 to 1.75 mm. Anterior end may be broader than posterior. Flat, not segmented, but with irregular transverse folds; ventral surface usually with distinct longitudinal median groove; dorsal surface may show two longitudinal grooves. Anterior margin rounded, with papilliform elevation, on which is found the head. The latter somewhat compressed and more or less invaginated.

HABITAT.—Superitoneal connective tissue and body cavity of man (*Homo sapiens*) and ? jackals (*Canis aureus*).

GEOGRAPHIC DISTRIBUTION.—Amoy and Japan; Daniels reports a similar, perhaps identical, form for Guiana, and Sonsino for Egypt.

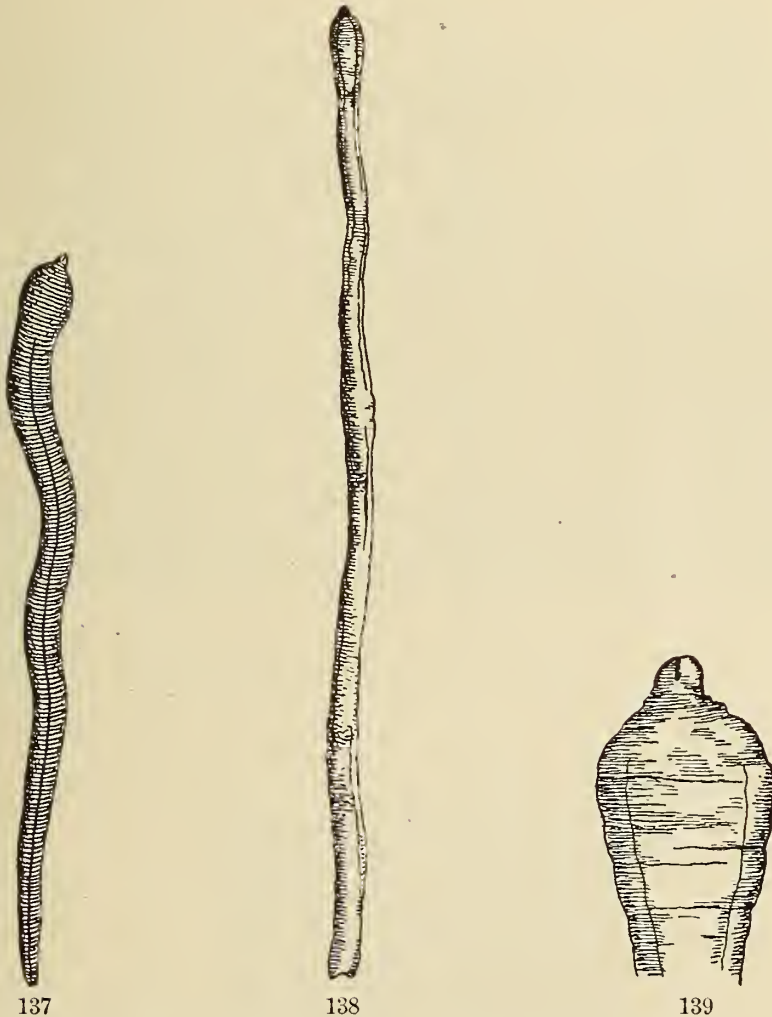


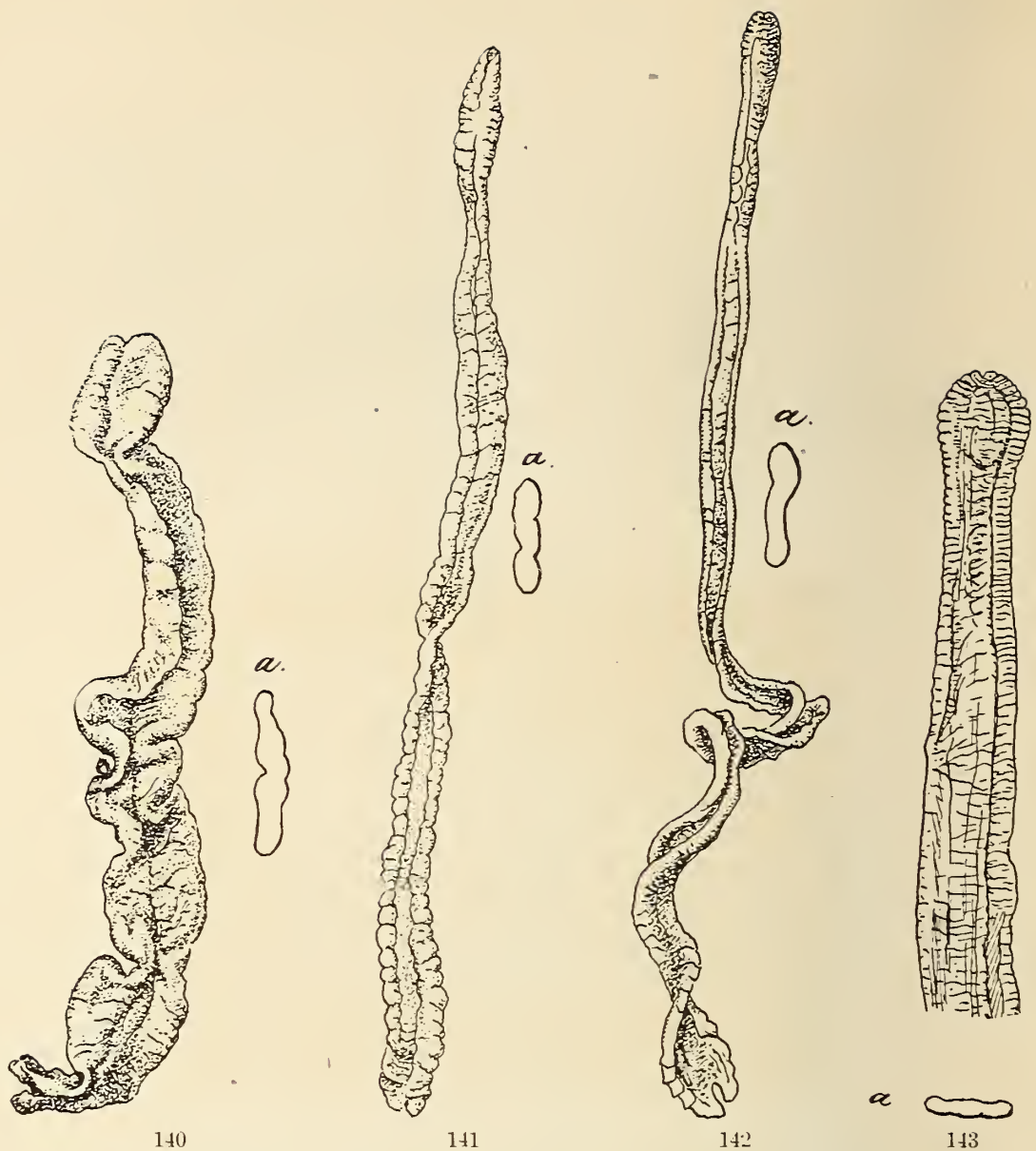
FIG. 137.—*Sparganum mansoni*. Natural size. (After Cobbold, 1883, fig. a.)

FIG. 138.—Another specimen of same. Natural size. (After Leuckart, 1886, 942, fig. 402a.)

FIG. 139.—Head end of same. $\times 5$. (After Leuckart, 1886, 950, fig. 405.)

^a **SYNONYMS.**—*Ligula mansoni* Cobbold in Manson, 1882; *Bothriocephalus liguloides* Leuckart, 1886; *B. mansoni* (Cobbold, 1882) R. Blanchard, 1888; *Legula mansoni* Cobbold of Huber, 1896a, misprint; *Bothriocephalus leguloides* Leuckart of Huber, 1896, misprint; *B. linguloides* Leuckart of Simon, 1897, misprint; *Dibothrium mansoni* (Cobbold, 1882) Ariola, 1900; *Leguli mansoni* Huber of Stiles & Tayler, 1902, misprint.

BIBLIOGRAPHY.—For full bibliography and compilation of cases see Stiles & Tayler, 1902, 47–56, figs. 29–36.



FIGS. 140 to 143.—Four different specimens of *Sparganum mansonii*: a., cross sections. Figs. 140 to 142 natural size; fig. 143 $\times 2$. (After Ijima & Murata, 1888a, figs. 1, 3, 4, 5.)

The Proliferating Japanese Tapeworm Larva—**SPARGANUM PROLIFERUM**^a
(Ijima, 1905) Stiles, 1906.

[Figs. 144 to 166.]

SPECIFIC DIAGNOSIS.—*Sparganum*: Larva may attain 1 to 12 mm. in length and 2.5 mm. in breadth; head narrower and more motile than posterior end, and may show an apical depression which, perhaps, serves as sucker; no true suckers or other organs of attachment present. Calcareous corpuscles spherical or ellipsoidal, 7.5 to 12 μ in diameter, and situated in any part of body except head; irregularly distributed reserve-food bodies present in older specimens, but they later undergo disintegration; genital organs not present; longitudinal muscles better developed than

^a**SYNONYMS.**—*Plerocercoides prolifer* Ijima, 1905; *Plerocercus prolifer* Ijima, 1905. Neither *Plerocercoides* (type *bailleti*) nor *Plerocercus* is available in naming this species. Because of the remarkable reproduction of the larval stage, a new genus would probably be justified, but there are some advantages in placing the worm, at least for the present, in the collective group *Sparganum*.

BIBLIOGRAPHY.—See Ijima, 1905.

either dorso-ventral or transverse system; transverse fibers do not divide body into cortical and medullary layers; excretory system well developed, consisting of larger approximately longitudinal branches, with anastomoses. The larvæ possess the power of multiplying by transverse fission and of forming supernumerary heads which may become independent. Adult unknown.

HABITAT.—Encysted in subcutaneous tissue and elsewhere of man.

GEOGRAPHIC DISTRIBUTION.—Reported but once, Tokyo, Japan.

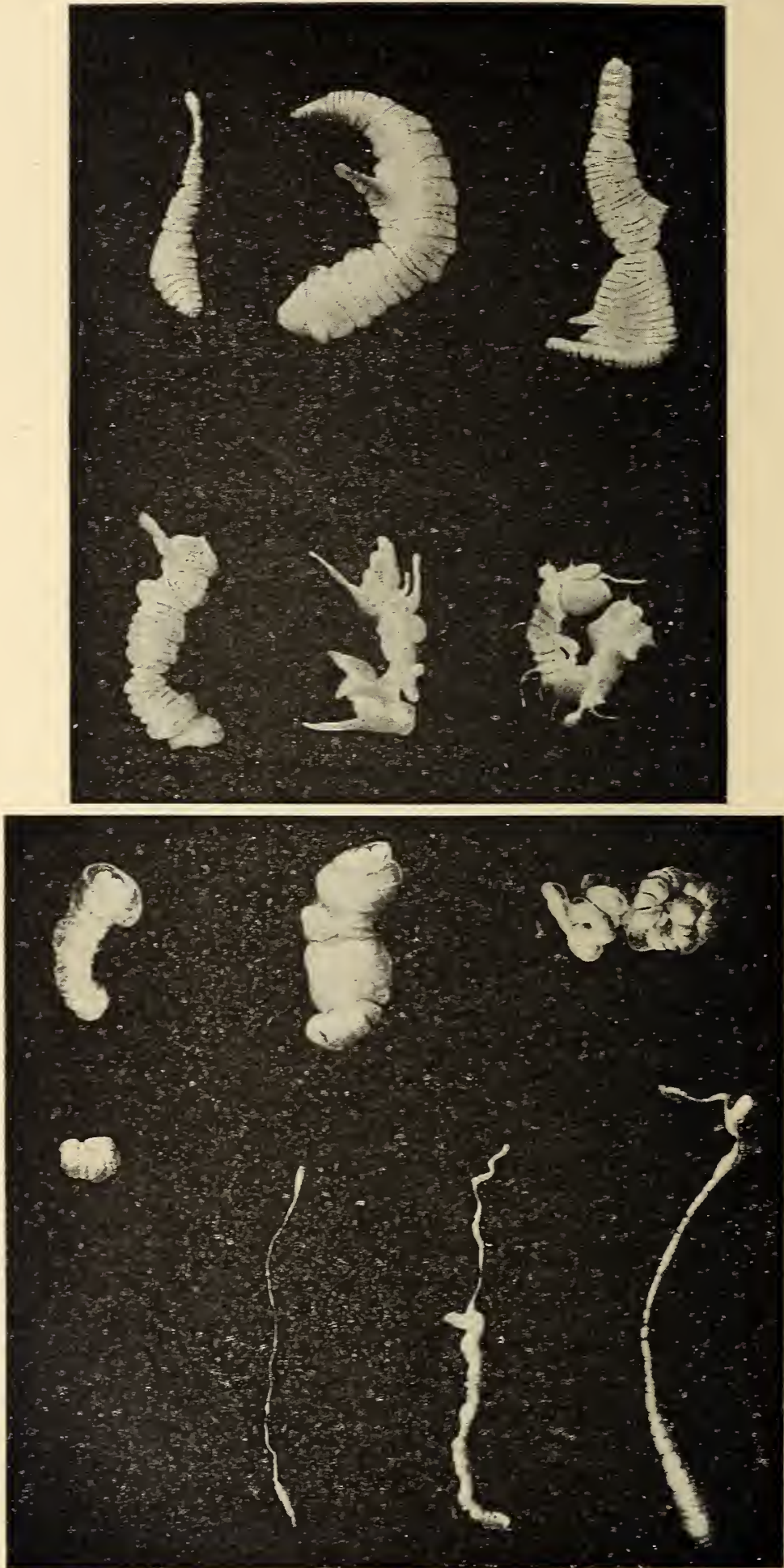
MEDICAL SIGNIFICANCE.—In the single case reported thousands of parasites were present; they gave rise to acme-like swellings, to an enlarged condition of the thigh resembling elephantiasis; and to their presence in the region of Poupart's ligament was attributed an inguinal hernia.



FIG. 144.—A vertical section of the skin and subdermal tissue from left thigh, showing numerous cysts of *S. proliferum*. (After Ijima, 1905, fig. 1.)



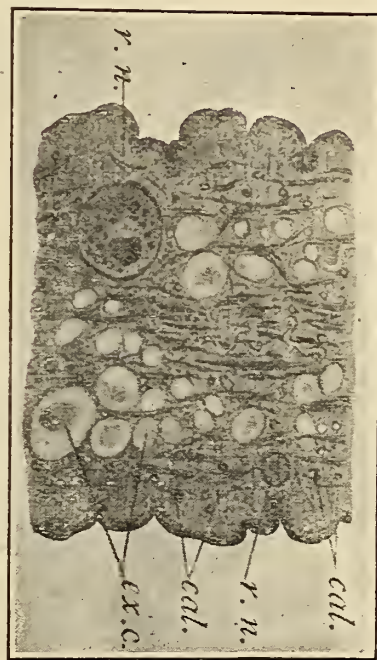
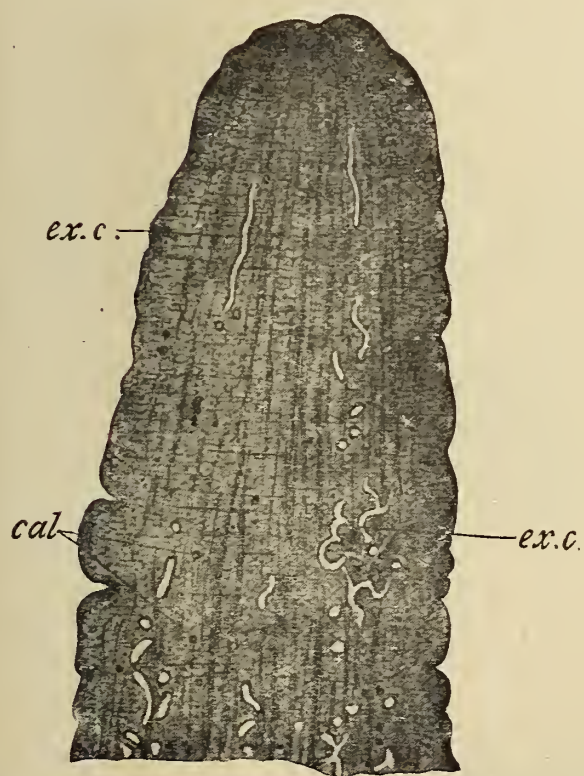
FIG. 145.—Seven separate pieces of *S. proliferum* taken from one cyst. $\times 1\frac{1}{2}$. (After Ijima, 1905, fig. 2.)



FIGS. 146-158.—Thirteen specimens of *S. proliferum* of various shapes; some show supernumerary heads. $\times 4$. (After Ijima, 1905, figs. 3-15.)



FIG. 159.—Transverse section of head region of *S. proliferum*: *ex. c.*, excretory canals; *n.*, lateral nerves. $\times 100$. (After Ijima, 1905, fig. 16.)



FIGS. 160-161.—Longitudinal section of (160) head and (161) near posterior end of *S. proliferum*: *cal.*, calcareous corpuscles; *ex. c.*, excretory canals. $\times 50$. (After Ijima, 1905, fig. 21.)

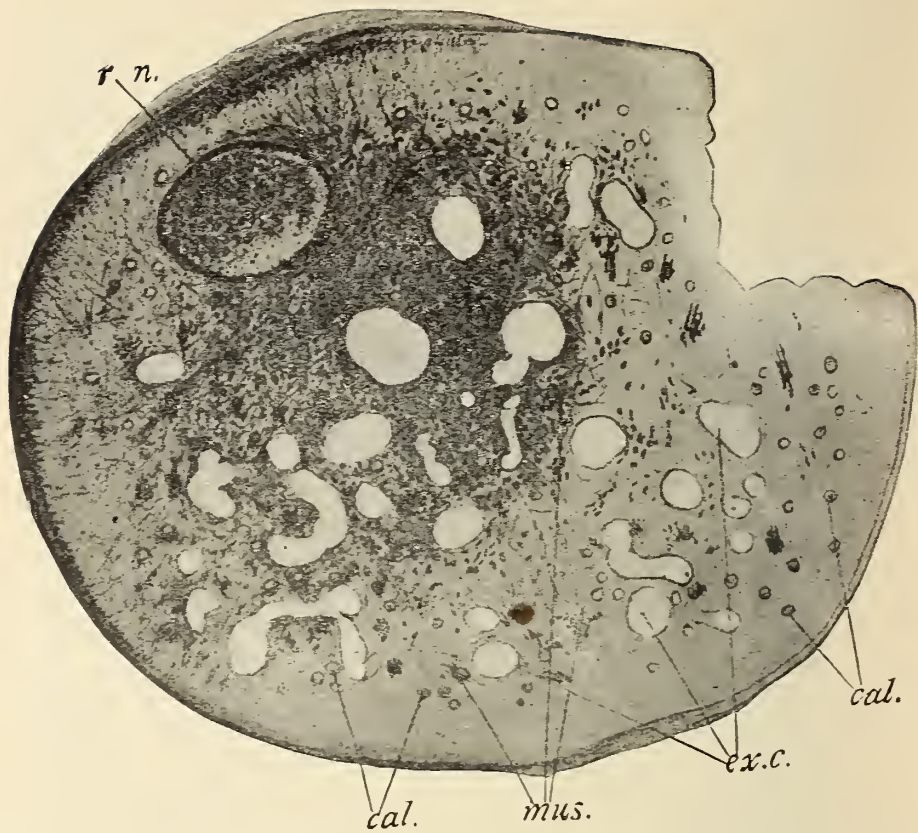


FIG. 162.—Transverse section of posterior portion of *S. proliferum*: *cal.*, calcareous corpuscles; *ex. c.*, excretory canals; *mus.*, muscles; *r. n.*, reserve nutritive material. $\times 100$. (After Ijima, 1905, fig. 17.)

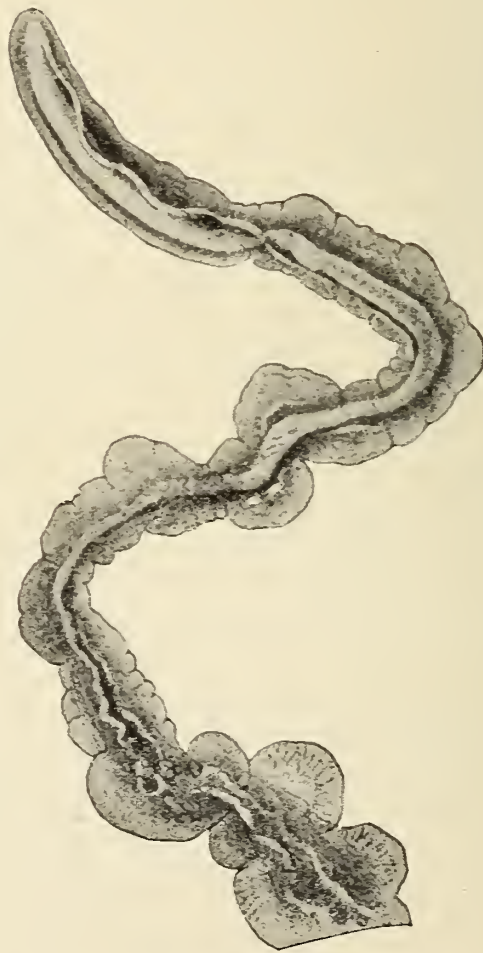


FIG. 163.—Head end of *S. proliferum* fully stretched; excretory vessel in part strongly swollen. $\times 30$. (After Ijima, 1905, fig. 18.)



FIG. 164.—An entire *S. proliferum*, overstained with carmine, then bleached with caustic potash; black dots represent calcareous corpuscles; *ex. c.*, excretory vessels; *r. n.*, reserve nutritive matter. $\times 30$. (After Ijima, 1905, fig. 19.)

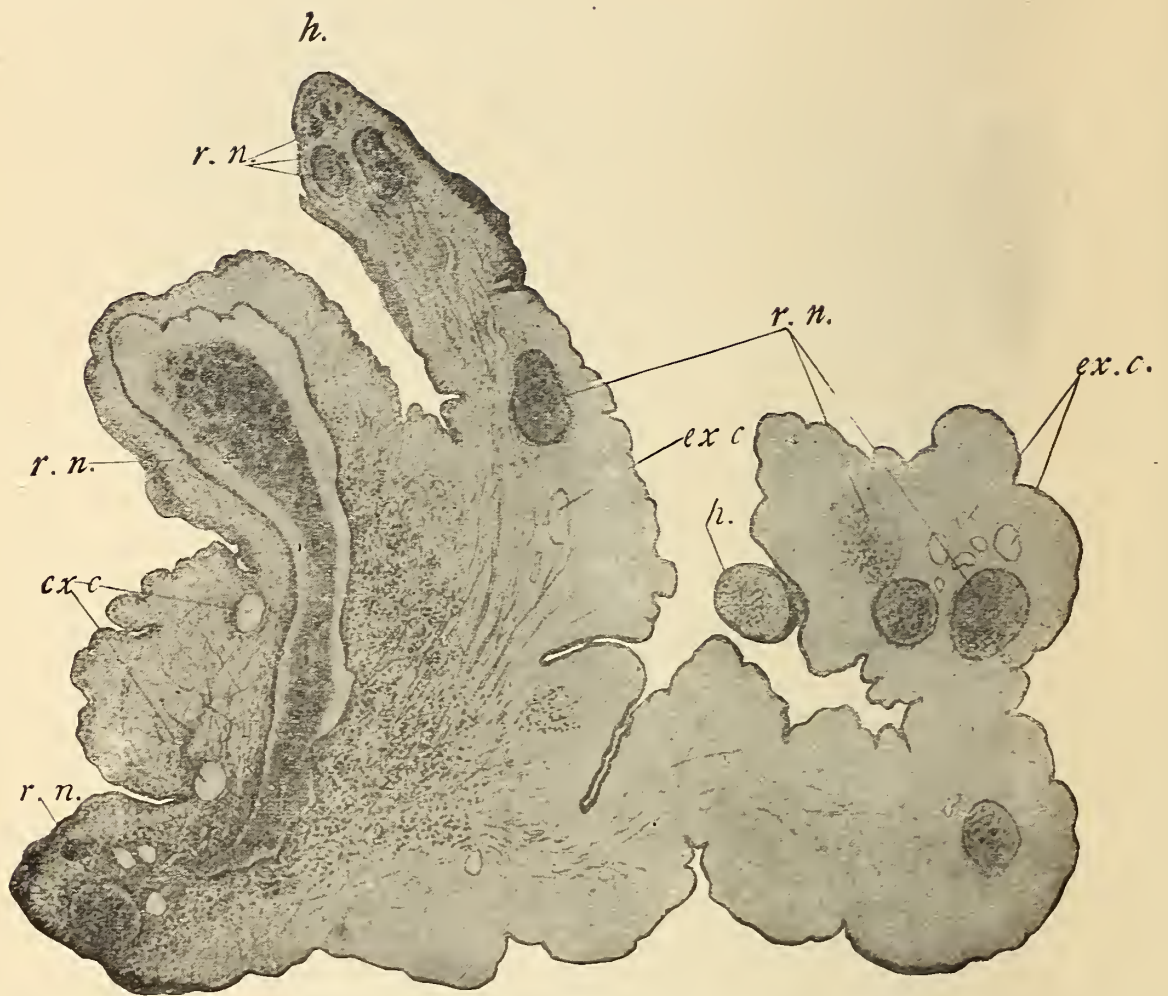


FIG. 165.—Section of budding *S. proliferum*, showing heads (*h*) in two places. $\times 50$. (After Ijima, 1905, fig. 20.)



FIG. 166.—Section of a cyst of *S. proliferum* in subdermal connective tissue. \times ca. 8. (After Ijima, 1905, fig. 23.)

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TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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M. J. ROSENAU, Director.

JANUARY, 1906.

ON THE STABILITY OF THE OXIDASES AND THEIR CONDUCT
TOWARD VARIOUS REAGENTS.

THE CONDUCT OF PHENOLPHTHALEIN IN THE ANIMAL
ORGANISM.

A TEST FOR SACCHARIN, AND A SIMPLE METHOD OF DISTIN-
GUISHING BETWEEN CUMARIN AND VANILLIN.

THE TOXICITY OF OZONE AND OTHER OXIDIZING
AGENTS TO LIPASE.

THE INFLUENCE OF CHEMICAL CONSTITUTION ON THE
LIPOLYTIC HYDROLYSIS OF ETHEREAL SALTS.

BY

J. H. KASTLE.



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ON THE STABILITY OF THE OXIDASES AND THEIR CONDUCT TOWARD VARIOUS REAGENTS.

By JOSEPH HOEING KASTLE, PH. D.,

Chief of Division of Chemistry, Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service.

THE STABILITY OF THE OXIDASES.

It has been observed that as a class the vegetable oxidases are extremely unstable substances. Fresh aqueous extracts of the potato, for example, rapidly oxidize guaiacum and phenolphthalin, but on standing at room temperature, in the presence of mild antiseptics, such extracts soon lose their oxidizing power. The same thing has been found to be true of plant oxidases from a great many other different sources.

During the past several years a number of fungi indigenous to central Kentucky and the District of Columbia have been examined with reference to their oxidizing power. As a general thing these observations have afforded nothing of particular interest.

In the case of the fungus *Lepiota americana*, however, the results would seem to indicate that, as compared with most vegetable oxidases, those present in this mushroom are unusually stable substances. In the young state this fungus is nearly white, with a few red spots on the pileus. With age, or as the result of injury, it becomes darker and of a more pronounced red color. On drying it finally turns to a dark brown or black mass, so dark, indeed, as to suggest that it has been charred. So far, then, as its general appearance is concerned, and the rapid development of pigment in its tissues, everything points to the presence of powerful oxidases in its juices.

With the view of determining its oxidizing powers a 10 per cent extract of the fungus was prepared by macerating the freshly gathered material with coarse white sand and water, using a small quantity of toluene as antiseptic. The filtered extract thus prepared was found to be deep wine red in color and to possess remarkable oxidizing powers. It gave a splendid guaiacum reaction with fresh tincture of guaiacum, and it also oxidized phenolphthalin much more rapidly than does any other preparation of plant oxidase that has ever come under

my observation. Control experiments with the boiled extract showed neither the oxidation of the guaiacum nor of the phenolphthalin. The chief point of interest connected with these observations, however, is that the extract of this fungus had not lost its oxidizing power at the end of four months. During this interval its oxidizing power was tested from time to time with the following results:

Date of observation.	Color with guaiacum.	Color with phenolphthalin.
Oct. 3, 1902	Deep indigo blue	Dark red.
Nov. 22, 1902do.....	Do.
Jan. 31, 1903	Dark blue.....	Red.
Feb. 5, 1903do.....	Do.

It has also been observed that the oxidases of the *Lepiota americana* are quite stable even in the presence of alcohol and formic aldehyde. That such is the case may be gathered from the following observations: On October 1, 1902, Professor Garman, of the Kentucky Agricultural Experiment Station, put up a specimen of the fungus in a preservative solution containing equal quantities of water and alcohol, together with 0.8 per cent of formic aldehyde. On standing in contact with the fungus the solution acquired a rich red-brown color. On December 1, 1902, some of the preservative fluid was removed from the specimen and tested for oxidases. It gave a splendid guaiacum reaction and also oxidized phenolphthalin.

On January 31, 1903, some of this same specimen of preservative solution that had been removed from the fungus on December 31 was again tested for oxidases. It gave a slight guaiacum reaction and oxidized phenolphthalin slowly. It therefore showed a remarkable falling off in oxidizing power as compared with the aqueous extract of the fungus. These results go to show, therefore, that whereas most plant extracts lose their oxidizing properties in several days—in fact, often in several hours—the extract of *Lepiota americana* retains its activity for weeks and months. In this connection an observation by Bourquelot on the oxidases of the *Russula delica* is not without interest. He found that the aqueous extract of this fungus when preserved in chloroform first loses its power to oxidize tyrosine, then the power to oxidize guaiacol, and finally, after eight weeks, the power to oxidize guaiacum. It would seem, therefore, that the most stable oxidases are those of fungi. Unfortunately the fungus, *Lepiota americana*, is rather rare in its occurrence in the locality mentioned, so that at the time that these first observations were made only a small amount of material was available for investigation.

On the 17th of August, 1904, however, several beautiful specimens of the fungus were obtained. With this material some further obser-

vations on the oxidases of this fungus have been made. In the first place, the earlier observations on the stability of the oxidases of this fungus have been confirmed. A 10 per cent aqueous extract of the fungus was prepared on August 17, 1904, and was found to be very active toward guaiacum. Some of this extract was kept in a glass-stoppered bottle in a dark closet at room temperature until January 2, 1905, when it was again tested with guaiacum. With this reagent it gradually developed a dark-blue color, whereas a control experiment, in which some of the extract had been boiled previously, showed no blue color on testing with guaiacum. With the old solutions of the fungus the blue color with the fresh tincture of guaiacum develops more slowly than with the fresh extract of the fungus. A glycerin extract of the fungus was also found to retain its power of bluing guaiacum practically unimpaired after four and one-half months. Such a glycerin extract was prepared on August 17 by macerating some of the fresh fungus with glycerin. At the time of its preparation this extract did not seem to possess quite as great oxidizing power as the aqueous extract. On January 2, 1905, a few drops of this glycerin extract were added to a small amount of water—about 1 cc.—and guaiacum added. In the course of a few moments it gave a deep indigo-blue color. From the facts as they are known at present it would seem that the oxidase of *Lepiota americana* is more stable in glycerin than in water.

With the view of learning still more as to the stability of the oxidases of the higher fungi, a number of these plants indigenous to the District of Columbia have recently been examined for oxidases. Aqueous and glycerin extracts of a number of fungi were prepared as soon as the material was collected. The aqueous extract was filtered and tested for oxidases by means of tincture of guaiacum and tincture of aloin, with the following results:

	Name of fungus.	Color with guaiacum.	Color with aloin.
1	<i>Lactarius piperatus</i>	Very dark blue instantly ...	Wine red.
2	<i>Russula emetica</i>	Dark blue	Pink, slow.
3	<i>Lactarius volumen</i>	Very dark blue instantly ...	Wine red.
4	<i>Volvaria bombycina</i>do	Deep wine red.
5	<i>Lactarius</i> , indigo	Dark blue	Do.
6	<i>Clitocybe ochropurpurea</i>	Very deep blue instantly ...	Pink.
7	Yellow fungus, undetermined.do	Wine red.
8	Small white variety, undetermined.do	Do.
9	<i>Agaricus campestris</i>	Light blue, slow	Colorless.
10	<i>Amanita verna</i>	Yellowish white	Do.

It is evident from these results that of the fungi thus far examined by far the greater number are rich in oxidases. The absence of oxidases from the highly poisonous mushroom *Amanita verna* is not

without interest, inasmuch as by means of the oxidase reagents here employed we can readily distinguish between this mushroom and many other species. While it would be premature to say that all mushrooms failing to give the oxidase reactions are poisonous, it can be said that any white-gilled fungus failing to show these reactions must be regarded with suspicion.

The glycerin extracts of these fungi prepared during the month of July were kept in the cold room—temperature= 15° C.—and practically in the dark until December 28, 1905, when they were again tested with guaiacum and aloin, with the following results:

No.	Name of fungus.	Color with guaiacum.	Color with aloin.
1	<i>Lactarius piperatus</i>	Very dark blue	Light red, slow.
2	<i>Russula emetica</i>	Light blue, slow	None.
3	<i>Lactarius volumen</i>	Dark blue	Deep-wine red.
4	<i>Volvaria bombycina</i>	None	Faint pink.
5	<i>Lactarius</i> , indigo	Dark blue	Wine red, slow.
6	<i>Clitocybe ochro-purpurea</i>	Light blue, darker on stand- ing.	Do.
7	Yellow fungus, variety un- determined.do	Do.
8	Small white fungus, variety undetermined.	Dark blue	
9	<i>Agaricus campestris</i>	Light blue, slow	None.
10	<i>Amanita verna</i>	None	Do.

It is clear from these results that at low temperatures, in the dark, glycerin extracts of certain fungi, notably *Lactarius piperatus*, *Lactarius volumen*, and the indigo lactarius retain their oxidizing powers practically undiminished for four months. On the other hand, certain of these, which in the fresh state possess remarkable oxidizing powers, such as *Volvaria bombycina* and the undetermined yellow species, No. 7, rapidly lose their power to effect the oxidation of guaiacum and aloin, even when carefully preserved in glycerin, at 15° C. As might be expected, the stability of the oxidases seems to be greatly influenced by the nature of the other substances with which they may happen to be in contact. Thus it has been found that they are less stable in water than in glycerin. Further, the stability of their aqueous solutions seems to be largely determined by the nature of the antiseptic with which such solutions are preserved. That such is the case may be gathered from the following observations:

Aqueous solutions of *Lactarius piperatus* and fungus No. 7 were prepared on August 4, 1905, and preserved in glass-stoppered bottles with small amounts of toluene, chloroform, and thymol, respectively, as antiseptics, in the dark at 15° C. These solutions were tested with guaiacum and aloin on December 28 with the following results:

Lactarius piperatus.

Antiseptic.	Color with guaiacum.	Color with aloin.
Toluene	Dark blue.....	Wine red.
Chloroform	None; light blue after long standing.	Faint pink.

Fungus No. 7.

Antiseptic.	Color with guaiacum.	Color with aloin.
Toluene	Dark blue.....	Light red.
Chloroform	Very light blue after standing	None.
Thymol	Faint blue after long standing	Do.

It is evident, therefore, that the oxidases of certain fungi are less readily destroyed by toluene than by chloroform or thymol.

With the material collected on August 17, 1904, I have been able to make out the following additional properties of the oxidases of *Lepiota americana*:

PRECIPITATION OF THE OXIDASE OF *LEPIOTA AMERICANA* FROM ITS
AQUEOUS SOLUTION BY MEANS OF ETHYL ALCOHOL.

Among other things, the attempt was made to obtain the oxidases of *Lepiota americana* in purer condition by precipitation with ethyl alcohol. Accordingly, to some of the perfectly clear 10 per cent aqueous extract of the fresh fungus there was added five or six times its volume of 95 per cent alcohol. The mixture soon became turbid, and in five or six minutes a brown flocculent precipitate made its appearance. This was allowed to settle and the liquid above it removed by means of a siphon as completely as possible. The remainder was then filtered and washed with 95 per cent alcohol. The residue was found to consist of a dark-brown colloidal material closely adhering to the filter paper. On drying in air it gave a black, shining deposit on the paper, which could be removed in the form of scales. This was found to be soluble in water, giving rise to a brownish-yellow solution, which on mixing with the tincture of guaiacum gave a splendid dark-blue color at once.

We see, therefore, that like many other ferments the oxidases of *Lepiota americana* are precipitable from their aqueous solution by alcohol in the form of a colloidal precipitate soluble in water. Some of this air-dried material was kept in the laboratory in the open air for four and one-half months. At the end of this time a small amount of it was rubbed up in a porcelain mortar with a few cubic centimeters of water; a reddish-brown solution was obtained, which gave a dark

indigo-blue coloration with guaiacum, whereas the boiled control gave no coloration with this reagent.

EFFECT OF HEAT ON THE OXIDASES OF *LEPIOTA AMERICANA*.

In the preceding part of this paper repeated reference has been made to the fact that the boiled controls of various extracts and preparations of the fungus gave no reaction with guaiacum.

It seemed of interest, therefore, to determine more carefully the effect of heat on the activity of the oxidases here under investigation. An aqueous solution of the alcoholic precipitate, described under the preceding head, was employed in these experiments. In order to determine the effect of heat on the activity of the oxidases, small bore test tubes containing 1 c.c. of the solution were immersed in water baths, the temperature of which was carefully regulated. After remaining in the bath for the desired interval, the tubes were removed and quickly brought to ordinary temperature and tested with guaiacum. The results of these observations are given in the following table:

Temperature.	Time of exposure in minutes.	Color with guaiacum.
80° C	5	Light blue.
80° C	10	Lighter blue.
80° C	30	Trace of blue.
80° C	60	None.
85° C	2	Faint blue.
85° C	5	Trace of blue.
85° C	10	None.
86° C	4	Do.
90° C	1	Do.
90° C	1	Trace of blue.
90° C	1	Do.
90° C	5	None.
90° C	10	Do.

At temperatures below 80° C., an hour's exposure was found to be insufficient to destroy the oxidizing power of this solution. It will be seen from our results, therefore, that the destruction temperature for the oxidases of *Lepiota americana* lies between 80° and 90° C., and that an exposure to a temperature of 80° C., for a comparatively short time, is insufficient to render these oxidizing substances inert.

The relatively high destruction temperature of these oxidases is in keeping with their remarkable stability at ordinary temperature. One of the tubes that had been exposed to a temperature of 90° C. for one minute was kept over night and then tested with guaiacum. It gave only a faint blue coloration with this reagent. We see, therefore, that after destruction by heat these oxidases show but little if any tendency to regain their activity. In other words, the destruction by heat seems to be permanent.

LÉPIOTA AMERICANA IN AIR AND HYDROGEN.

We have seen that the presence of these powerful oxidases in this fungus is closely associated with the development of its splendid red color. Such being the case, it occurred to me that it would not be without interest to observe its changes in an atmosphere of air and hydrogen. Accordingly a freshly cut piece of the pileus of a young specimen of the fungus, the gills of which were practically white, was sealed up in a tube in an atmosphere of hydrogen, while another similar piece of the same fungus was sealed up in a tube in an atmosphere of air, due precaution being taken, of course, not to injure the specimens of fungus by heat. Even after six hours it was evident that the specimen in hydrogen was decidedly whiter and less altered in appearance than the specimen which had been kept in air.

These two tubes were kept in a dark closet at ordinary temperature for three days. At the end of this time the two specimens presented a markedly different appearance. The specimen in hydrogen was white, with a small amount of clear yellowish exudate in the tube. The specimen in air was dark brown in color, black in spots, and the exudate was coffee colored. On opening the tube filled with hydrogen, a distinctly cheesy odor was perceptible and both the fungus and the clear yellow exudate rapidly took on the beautiful rose-red color characteristic of the more highly colored parts of the young fungus itself. This in itself shows that the natural color changes occurring in the fungus are the result of oxidation. The conduct of the clear yellowish exudate toward guaiacum proved to be exceedingly interesting. On adding tincture of guaiacum, the characteristic blue color showed itself at once. On shaking the solution, however, the blue color showed a tendency to disappear; but on allowing the liquid in the tube to come to rest the deep indigo-blue coloration of the guaiacum developed on the upper surface of the liquid, the depth of the blue zone depending on the time of exposure to the air. The middle layer of the liquid exhibited various shades of color, varying through dirty shades of blue and green, and finally the lower layer of the liquid took on a salmon-pink tint, the color of the exudate originally after a brief exposure to the air.

The phenomenon first brought about by shaking the liquid and allowing it to come to rest could be repeated at will, and always on standing the three differently colored layers made their appearance—the top, dark blue, the middle, greenish blue, and the lowest layer, pink. In order to show conclusively that the production of the guaiacum blue was brought about by the action of the atmospheric air, acting through the oxygen carriers present in the original exudate, a small amount of the lower layer was pipetted off and transferred to a small-bore glass tube in such a way as to inclose a bubble of air. Under

these conditions, two dark-blue zones were to be seen, one in contact with the bubble of air and one in contact with the air filling the upper portion of the tube. On opening the tube containing the fungus that had been kept in air it was found to have a yeasty smell, and a small portion of the fungus itself was found to have an acid reaction. The brown exudate gave a blue coloration with guaiacum, and a portion of the fungus, after maceration and extraction with water and filtration, gave a clear reddish-colored solution which gave a splendid guaiacum reaction which showed no tendency to change in any way. It will be observed, therefore, that the conduct of the exudate and the extract here obtained was altogether different from that obtained with the exudate and the extract from the fungus that had been kept in an atmosphere of hydrogen.

Evidently, therefore, when the fresh fungus is kept for some time in an atmosphere of hydrogen, there are produced reducing substances sufficiently powerful to reduce guaiacum blue. Whether these are the products of anærobic bacteria or of the fungus itself yet remains to be determined.

ON THE CONDUCT OF THE OXIDASES OF *LEPIOTA AMERICANA* TOWARDS VARIOUS SOLVENTS.

It has already been pointed out in a previous part of this communication that this fungus gave up its oxidases to a preservative solution consisting of equal quantities of water and alcohol, containing a small amount of formic aldehyde, and that such a solution retained its activity for two or three months. It therefore occurred to me that it would not be without interest to study the stability and conduct of the oxidases of *Lepiota americana* toward various solvents. Accordingly, the pileus of perfectly fresh specimens of the fungus, the gills of which were either white or slightly greenish, was cut into pieces about an inch long by one-fourth of an inch thick and broad. These pieces were then immersed completely in the solvent the effect of which it was desired to study, and the solvent containing the fungus sealed up in a glass tube.

The following solvents were studied: Water, ethyl alcohol, amyl alcohol, allyl alcohol, glycerin, formic aldehyde, chloral hydrate, and a mixture of toluene and water.

In water, ethyl alcohol, amyl alcohol, and glycerin, the fungus was found to take on a beautiful rose-red color, particularly the gills. This finally changes to a brownish-red tint. After standing a short time under allyl alcohol, the pileus showed a more decided red color. On the other hand, formic aldehyde and chloral hydrate differ from the solvents just mentioned in the sense that they, like hydrogen, tend to bleach the fungus.

These specimens were placed under these several solvents on August 17. On August 21 the specimens were again examined, and the solutions thus obtained and also the pieces of fungus under these several solvents were tested with tincture of guaiacum with the following results:^a

(1) The aqueous solution was found to be deep brown in color, and 1 c.c. of the solution gave a very deep indigo-blue color with guaiacum. A portion of the fungus that had stood under water was removed from the solution, washed with water, macerated with water, and filtered. A portion of the filtrate gave a distinct blue with guaiacum, but by no means was the same depth of color obtained as with the original aqueous solution, indicating that the greater part of the oxidase had passed into solution in the first portion of water. A remarkable solubility in water seems to be a general characteristic of the vegetable oxidases.

(2) The alcoholic solution was found to be reddish brown in color, and gave no test for oxidase with guaiacum. On the other hand, a portion of the fungus that had stood under alcohol gave on maceration with water an aqueous solution, which gave a splendid reaction with guaiacum.

(3) The solution in amyl alcohol was found to be dark brown in color and the piece of fungus itself nearly black in places. The solution gave no reaction with guaiacum, or at the most only a trace. The fungus which had stood under amyl alcohol gave on maceration with water a clear, yellowish-red solution. This with guaiacum gave a dark-blue coloration.

(4) In allyl alcohol the fungus gave a pinkish solution, whereas the fungus itself remained nearly white. The solution gave no reaction with guaiacum, whereas the aqueous extract of the fungus itself was clear and slightly pink in color, and gave a good reaction with guaiacum, though somewhat slow in developing.

(5) The solution in 40 per cent formic aldehyde was wine red in color and clear. It gave an excellent reaction with guaiacum. The fungus itself was nearly white. On maceration with water, it yielded a slightly pink clear solution, which gave only a slight reaction with guaiacum.

(6) A concentrated solution of chloral hydrate gave, on standing in contact with the fungus, a brownish solution, which gave no reaction with guaiacum. The fungus itself was nearly white, and on maceration with water yielded a pink extract, which also gave no reaction with guaiacum. The oxidase, therefore, seems to be entirely destroyed by chloral hydrate.

^aIn this connection the aqueous solution of *Lepiota americana* was also tested for nitrites with negative results. In a general way this confirms the observation by Bach, who, as opposed to Aso, found no evidence of nitrites in the oxidases of plants which he examined.

(7) On standing in contact with glycerin, a portion of the glycerin became dark coffee-brown in color. The glycerin extract gave splendid reactions with guaiacum, both alone and on mixing with water. The fungus itself became brownish black in color, and on maceration with water it gave a reddish-brown extract, which was found to give a very decided reaction with guaiacum.

(8) On standing in contact with equal amounts of water and toluene until August 22, 1904, the layer of toluene became clear lemon yellow, whereas the aqueous layer became clear reddish brown. Some of the toluene was carefully drawn off by means of a pipette and shaken up with a small amount of water in a test tube. The water at once became reddish brown in color, and on adding guaiacum it developed a deep blue coloration at once. Some of the toluene was then added to an equal amount of water in a test tube and the mixture shaken. On standing for a short time the mixed liquid separated into two layers, a reddish-brown aqueous layer and a clear lemon-yellow layer of toluene. Some of the lower layer was withdrawn by means of a pipette and tested with guaiacum. It also gave a deep indigo-blue coloration immediately. On the other hand, when a large amount of water was employed to extract the oxidase from its solution in toluene, the aqueous solution became pink in color, but failed, for some reason unknown to me at present, to give the guaiacum reaction. The aqueous portion of the original solution was found to be exceedingly active—one drop of its solution giving a good guaiacum reaction when diluted to 3 cubic centimeters with water.

Several conclusions may be drawn from these results:

(1) That the oxidase of *Lepiota americana* is much more readily soluble in water than in any other solvent.

(2) That even in solution the oxidase is not destroyed by 40 per cent formic aldehyde.

(3) That while it does not dissolve in ethyl, amyl, or allyl alcohol, it is not destroyed by contact with these substances.

(4) That it is soluble in glycerin and apparently, to some extent at least, in toluene. Whether the perfectly dry oxidase is soluble in toluene remains to be proved. It may be, of course, that it is the water which is dissolved in the toluene which really takes the oxidase into solution. This point requires further investigation. It is certain, however, that when water and toluene are both present a part of the oxidase passes into the toluene layer.

(5) That certain substances, such as chloral hydrate, destroy the oxidase completely.

REAGENTS FOR THE OXIDASES.

Several years ago O. M. Shedd and myself^a called attention to the fact that phenolphthalin could be employed advantageously as a reagent

^a Am. Chem. Jour., XXVI, 1901, 526-539.

for the oxidases. Since then similar studies have been carried out with various other leuco compounds and chromogenic substances. The following are the more important results that have been reached in these investigations:

Leuco-rosolic acid.—The oxidation of this compound by certain plant oxidases has been studied by G. F. Mason and myself. The former obtained this compound in the form of beautiful transparent, colorless needles. In order to test its conduct toward the plant oxidases, a small amount of it was dissolved in a slight excess of sodium hydroxide. Two tubes were then prepared: No. 1 contained 1 cc. of the solution of leuco-rosolic acid, together with 5 cc. of a freshly prepared aqueous extract of the skin of the potato; No. 2, same as No. 1, except that the aqueous extract of the potato had been boiled and then cooled to room temperature before it was mixed with the reagent. After standing one hour at ordinary temperature, 0.15 cc. N 5 sodium hydroxide solution was added to each tube. No. 1 became dark purplish red immediately, whereas No. 2 showed no trace of pink or red color. It was also observed that the potato oxidase oxidizes leuco-rosolic acid most rapidly in faintly alkaline solutions. Acid solutions and more strongly alkaline solutions of the compound were scarcely oxidized at all.

Ethyl phenolphthalin.—This compound was prepared by Mason according to Baeyer's directions. In order to test its conduct toward the oxidases, tubes were prepared containing 5 cc. of active and boiled aqueous extract of the skin of the potato, respectively. To these tubes small amounts of ethyl phenolphthalin were added. At the end of 30 minutes the tube containing the active extract developed a purple-red coloration on the addition of the alkali, whereas the boiled control gave only a slight yellowish-brown coloration. Other tubes were allowed to stand 18 hours. These showed a still more marked difference in color on the addition of alkali.

Ethyl tetrabromphenolphthalin.—This compound was also prepared by Mason according to the method of Baeyer. It was found to be far more difficult to oxidize than the ethyl ester of phenolphthalin. In fact, with potato oxidase we did not succeed in oxidizing it at all, whereas on standing with certain of the organic peroxides, such as benzoyl peroxide and benzoyl acetyl peroxide (acetozone), it was oxidized with the production of a bluish-green coloration, but only slowly. The presence of bromine in this compound seems in some way to inhibit its oxidation by plant oxidases.

Alcin.—A solution of this substance in alcohol and in an aqueous solution of chloral hydrate together with ozonized turpentine or hydrogen peroxide has been employed by Klunge and later by Schaer as a blood test. It would also appear from the work of Schaer that this substance is a general reagent for the peroxidases. Whether

Schaer made use of it as a reagent for the oxidases, however, I have been unable to determine from an examination of the literature at present accessible. It therefore occurred to me that this substance might prove to be a very beautiful and delicate reagent for the oxidases.

With the view of testing the conduct of aloin toward the oxidases, the following solutions of this substance have been prepared:

Alcoholic aloin.—This solution was prepared by dissolving 0.25 to 0.5 grams of powdered aloin in 50 cc. of 95 per cent alcohol. In some of our observations this solution was made use of without further treatment or modification. Generally, however, it was shaken with a small amount of zinc dust and filtered, inasmuch as it was found that such treatment considerably increased the sensitiveness and delicacy of the reagent. A solution of powdered aloin in a 10 per cent aqueous solution of chloral hydrate has also been employed, and in all cases these two solutions have been employed side by side with alcoholic guaiacum by way of comparison. In carrying out the tests, 2 or 3 cc. of an aqueous solution or extract of the material to be tested was brought together with from 0.1 to 1 cc. of the reagent, and the color change, if any, noted. Among others, the following plants have been examined both with aloin and guaiacum:

Name of plant.	Part examined.	Guaiacum.	Color produced with reagent.	
			Alcoholic aloin.	10 per cent chloral aloin.
Potato, <i>Solanum tuberosum</i> .	Tuber	Deep blue.	Deep wine red.	Deep wine red.
Eggplant, <i>Solanum melongena</i> .	Fruit	do	do	Do.
Sweet potato, <i>Ipomæa batatas</i> .	Tuber	do	do	Do.
Dandelion, <i>Taraxacum officinale</i> .	Leaves	do	do	Do.
<i>Lactarius piperatus</i>	Whole fungus..	Very dark blue.	Wine red..	Wine red.
<i>Lactarius volumen</i>	do	Deep blue..	do	Do.
<i>Lactarius indigo</i>	do	do	Deep wine red.	Deep wine red.

Still other fungi, as yet not certainly identified, have also given excellent tests for oxidases both with guaiacum and aloin. It will be observed therefore that the parallelism between the guaiacum and aloin reactions is complete. Without entering further into details, it may be said that so far as the delicacy of the reagent is concerned guaiacum and aloin are very nearly equal. Toward the oxidases of certain plants guaiacum seems to be a trifle more sensitive than aloin, whereas with others the converse is true. However, there are certain advantages attaching to aloin as a reagent for the oxidases which put it ahead of guaiacum. In the first place, the red coloring matter produced

by the oxidation of the aloin is much more stable than the blue compound produced by the oxidation of the guaiacum. Secondly, the red coloring matter resulting from the oxidation of the aloin is soluble in water and in aqueous extracts containing the oxidases. It has been found, therefore, that alcoholic aloin is a very delicate reagent for oxidases, especially when it is poured into the tube containing the aqueous extract of the plant in such a way as to prevent the mixing of the two liquids.

Under these circumstances the aloin takes on a red color at the zone of contact of the two solutions, and in this manner it has been found possible to recognize very small amounts of oxidases, such small amounts indeed that their presence in the solution would have been doubtless overlooked by the ordinary methods employed in testing for these substances. On the other hand, as a reagent for the oxidases, aloin also possesses certain disadvantages; especially is this true of the alcoholic solution that has been treated with zinc dust. While such solutions become very sensitive after a short exposure to the air, after several days' exposure they seem to lose their power of reacting with the oxidases altogether. That such is the case is evident from the conduct of the following aloin solutions toward fresh aqueous extracts of the horse-radish, *Nasturtium armoracia*:

- (1) Freshly prepared alcoholic aloin.
- (2) Same as (1), except that it had been shaken with zinc dust and filtered.
- (3) Same as (2), except that it had been prepared several days before being used.

0.5 cc. of solutions (1) and (2) and (3), respectively, were added to 2 cc. of a freshly prepared aqueous extract of horseradish root with the following results:

- (1) Remained yellow after standing.
- (2) Light reddish-brown in color, lighter than (3).
- (3) Wine red.

These results were duplicated in another extract.

The activity of these solutions was also tested toward a fresh aqueous extract of potato oxidase, with the following results:

- (1) Color quite slow in developing—faint pink.
- (2) Deep wine-red, almost instantly.
- (3) Followed (2) in order of activity.

Control experiments with the boiled extract of the potato gave only a slight pink with (2) on standing for some time. Finally an alcoholic solution of aloin that had stood at room temperature for two days, and which originally had been found to be very active toward oxidases, was found to have become reddish-brown in color and to have lost its activity toward oxidases to a great extent. It would seem, therefore, that aloin is very much like guaiacum, in the sense that on

standing exposed to the air its alcoholic solutions become more sensitive to oxidation by plant extracts. This can be readily accounted for on the supposition that on standing exposed to the air alcoholic solutions, both of aloin (particularly those which had been shaken with zinc dust) and guaiacum, absorb small amounts of oxygen with formation of peroxides of some description, and that in the presence of the latter peroxidases, as well as oxidases, react to form the coloring matter when such old solutions are brought in contact with plant extracts. In support of this conception may be mentioned the fact that aqueous solutions of the horseradish give no blue color with fresh tincture of guaiacum alone, whereas, as pointed out by Bach, this plant is particularly rich in peroxidases. Hence it is very important to employ fresh solutions of aloin if correct conclusions are to be reached as to the presence or absence of oxidases in the extracts of living tissues. With ordinary precautions, however, aloin is an excellent reagent for the oxidases.

THE ALOIN PEROXIDASE REACTION.

As stated above, aloin, together with ozonized turpentine or hydrogen peroxide, has been employed by Klunge and also by Schaer as a test for blood. This reaction undoubtedly depends on the presence of a peroxidase in the blood. With a solution of aloin in chloral hydrate and a 3 per cent solution of commercial hydrogen peroxide small quantities of the blood of a guinea pig produce a deep, wine-red coloration, which remains permanent for a considerable time. From a few preliminary observations with plant extracts, however, it appeared that aloin and hydrogen peroxide did give the peroxidase reaction. In order to test this point more thoroughly the following experiments were carried out with aqueous extracts of the fresh root of the horse-radish, which, according to Bach, is particularly rich in peroxidase.

The fresh aqueous extract of horse-radish gave no reaction with guaiacum. On the other hand, with 3 per cent hydrogen peroxide and guaiacum, it gave a deep blue coloration, but with aloin and some of the same hydrogen peroxide it gave no coloration at all. It therefore occurred to me to repeat the work of Schaer on the peroxidase reaction with aloin and hydrogen peroxide, as furnished by extracts of the poke, *Phytolacca decandra*. Accordingly some of the leaves of this plant were mascerated with water and filtered. To the filtrate chloroform was added and the solution allowed to stand overnight. On the following morning it was again filtered, whereby a clear, yellowish solution was obtained. This solution gave no test for oxidases, either with guaiacum or with the aloin solutions that had been employed throughout this work. On the other hand, on adding a small amount of a 3 per

cent solution of hydrogen peroxide to some of the clear extract, and then aloin or guaiacum, a good test for peroxidase was obtained with both reagents.

It was further shown by these experiments on the clear extract of *Phytolacca decandra* that better peroxidase reactions could be obtained with aloin by using very small amounts of hydrogen peroxide. In order to test this point more thoroughly five tubes were prepared, each containing 2 cc. of the aqueous extract of *Phytolacca decandra*. To (1) there was added no hydrogen peroxide, to (2) 0.1 cc. of hydrogen peroxide, to (3) 0.2 cc., to (4) 0.3 cc., and to (5) 0.4 cc. of 3 per cent hydrogen peroxide. To each of these tubes there was then added 0.5 cc. of a solution of aloin in 10 per cent chloral hydrate solution with the following results:

1. Yellow in color.
2. Very deep wine-red.
3. Wine-red, lighter than (2).
4. Red, lighter than (3).
5. Light pink, lighter than (4).

These experiments were repeated, using 3 per cent hydrogen peroxide that had been diluted with ten volumes of water. With hydrogen peroxide of this dilution no great differences were observable in the color of the tubes, all of them except (1) being deep wine-red. These results go to show that the intensity of the aloin peroxidase reaction, as shown by *Phytolacca decandra*, is clearly dependent on the concentration of the hydrogen peroxide, and but little differences are observable in the intensity of the reaction, provided very small amounts of hydrogen peroxide are employed. It therefore seemed to be advisable to repeat the work on the extract of the horse-radish, using hydrogen peroxide of greater dilution than had hitherto been employed. Accordingly, a fresh aqueous extract of the root of the horse-radish was prepared. With this four tubes were prepared, each containing 2 cc. of the extract. To these the following amounts of 0.3 per cent hydrogen peroxide were added: To (1), none; to (2), 0.1 cc.; to (3), 0.2 cc.; to (4), 0.3 cc. To each of these tubes there was then added 0.5 cc. of a solution of aloin in 10 per cent chloral hydrate, with the following results:

- (1) Yellow in color.
- (2), (3), (4) became deep wine-red, in the order named.

Similar experiments were carried out with an aqueous extract of the skin of the potato, which had stood several hours and which had lost the power to give the guaiacum reaction for oxidases. With this extract three tubes were prepared, using 2 cc. of the extract. To these the following amounts of 0.3 per cent hydrogen peroxide were added: To (1), none; to (2), 0.1 cc., and to (3), 0.2 cc. To each tube

there was then added 0.5 cc. of a solution of aloin in 10 per cent chloral hydrate. (1) remained yellow in color, (2) became wine red, and (3) also became wine red in color, but more slowly than (2). These results tend to confirm the work of Schaer on the use of aloin as a reagent for the plant and animal peroxidases. At the same time they go to show that the delicacy of this test for the plant peroxidases depends very largely on the concentration of the hydrogen peroxide, and that as a rule much better results are obtained by the use of small amounts of the peroxide. On the other hand, with the peroxidases of the animal tissues larger amounts of the hydrogen peroxide can be employed with good results.

THE CONDUCT OF PHENOLPHTHALEIN IN THE ANIMAL ORGANISM.

Several years ago Kastle and Shedd^a proposed the use of phenolphthalin, dioxytriphenylmethane carbonic acid, as a reagent for the oxidizing ferments. By means of the vegetable oxidases this compound is readily oxidized to phenolphthalein. On the other hand, all attempts to oxidize this compound with extracts of animal tissues have resulted thus far in failure, and even when injected into the animal subcutaneously it passes apparently unchanged into the urine, and but little, if any, of it is oxidized to phenolphthalein. In the light of this fact, it occurred to me to ascertain whether the reverse of this change could be effected in the animal organism; that is, whether phenolphthalein could be reduced to phenolphthalin. That powerful reductions are accomplished in the animal organism is indicated by the work of Ehrlich,^b who showed that in the living animal various animal tissues can effect the reduction of indophenol and alizarin blue to their corresponding leuco-compounds. With the view, therefore, of determining whether phenolphthalein could be reduced in the organism, on October 16, 1905, 0.5 gram of the compound was made into a suspension in water and injected into the peritoneal cavity of a guinea pig weighing 325 grams.

Apparently the injection caused no serious discomfort, and, except for some diuresis and some loss in weight, no unfavorable symptoms were observable at any time, and the animal is alive and apparently well at this time, viz, December 30, 1905. In one hour after the injection a specimen of the urine of the animal was obtained. This gave no test for phenolphthalein or phenolphthalin, nor for any conjugation product of either of these compounds. During the night of October 16 the pig passed a considerable quantity of urine. This was normal in appearance and gave no red color for phenolphthalein on the addition of caustic soda. Some of it was then boiled for a few minutes with dilute hydrochloric acid. This was then cooled and made alkaline with caustic soda, when the characteristic purplish red color of phenolphthalein in alkali was obtained. This would seem to indicate that phenolphthalein, when injected into the peritoneal cavity of an animal, forms some conjugated compound, which of itself gives no color reaction with caustic soda, but which is hydrolyzable by hydrochloric acid, yielding phenolphthalein as one of the products of the hydrolysis.

^a Am. Chem. Jour., XXVI, 526-539.

^b "Das Sauerstoff Bedurfniss des Organismus." Berlin, 1885.

Between 9 and 10 a. m., October 17, the animal passed another portion of clear urine. This also was normal in appearance and gave no evidence of phenolphthalein on the simple addition of caustic soda, but on boiling with dilute hydrochloric acid the acid solution of the urine took on a very decided blue color, and on cooling and making alkaline with caustic soda the characteristic purplish-red coloration of phenolphthalein in alkali was obtained. From this time on until November 20, 1905, the urine of this pig was tested several times each day in the manner already described, using from 1 to 5 c.c. of the urine for each test. At no time, however, during this interval did the urine show more than the faintest trace of pink color on the addition of caustic soda direct and frequently none at all. On boiling the specimen with dilute hydrochloric acid, however, and then adding caustic soda a very decided purplish-red coloration was obtained with each sample of urine for a period of nineteen days, and distinct traces of the phenolphthalein compound were recognizable in the urine as late as November 20, 1905.

In order to determine whether any phenolphthalein is reduced in the organism a specimen of the urine of pig (1), which was nearly colorless, was filtered and divided into two equal portions. To one of these (1) there was added 0.5 cc. of water, and to the second (2) 0.5 cc. of a solution of potassium ferricyanide. To each of these solutions 0.3 cc. of 2N sodium hydroxide was then added. The color change brought about by the addition of the sodium hydroxide to (1) was very slight, whereas in the case of (2) the solution became distinctly reddish, indicating the presence in the urine of a leuco-compound oxidizable by potassium ferricyanide. This substance in all probability is phenolphthalin. Compared with the amount of phenolphthalein, however, which is recoverable from the urine by hydrolyzing it with hydrochloric acid, the quantity which is reduced to phenolphthalin in the organism is practically negligible.

THE CONDUCT OF OTHER PHTHALEINS IN THE ANIMAL ORGANISM.

Fluorescein.—The conduct of fluorescein in the animal organism was also tested on a guinea pig in the following manner: 0.5 gram of fluorescein, suspended in water, was injected into the peritoneal cavity of a guinea pig weighing 455 grams at 2 p. m., October 17, 1905. In less than an hour the animal was completely prostrated and showed a tendency to convulsive movements. The animal died at 3.45 p. m. of the same day. Sometime after the injection the eyes of the pig exhibited a marked greenish fluorescence.

The post-mortem examination showed all of the internal organs to be strongly colored with fluorescein. The skin also was greenish yellow and all parts of the eye contained fluorescein, except the crystalline lens. The peritoneal cavity contained considerable fluid. The blad-

der was found to be nearly empty. It was removed, however, and put in a small amount of water. To some of the solution of the bladder contents thus obtained caustic soda was added. The alkaline solution thus obtained was practically colorless, or very faintly yellow by transmitted light, and by reflected light exhibited a slight greenish fluorescence.

A second portion of the solution of the bladder contents was boiled with dilute hydrochloric acid, then cooled and made alkaline with caustic soda. The solution thus obtained was decidedly orange yellow by transmitted light, and by reflected light exhibited a very marked greenish fluorescence. The liver of the pig was removed and washed several times with physiological salt solution. It was then preserved in normal salt solution by means of toluene over night. The next day it was examined in the following manner:

1. 0.1 gram of the liver was ground to a paste in a porcelain mortar and boiled with 10 cc. of water, and made up to 25 cc. This mixture was then filtered.

2. 0.1 gram of the liver was ground to a paste and boiled with 5 cc. of water and 5 cc. of dilute hydrochloric acid. This was then made up to 25 cc. and filtered.

Filtrates of (1) and (2) were compared as to fluorescence, by adding sodium hydroxide to equal amounts of the two filtrates; (1) was found to be only faintly fluorescent, whereas (2) was found to be strongly fluorescent and by transmitted light showed a deeper orange-yellow color than (1).

Ten cc. of filtrate (1) was boiled with a small amount of dilute hydrochloric acid, evaporated somewhat, and then cooled and made up to a total volume of 10 cc. Sodium hydroxide was then added to this solution and also to 10 cc. of (1). The former showed a decidedly greater fluorescence than (1).

It would seem, therefore, that while fluorescein is more rapidly absorbed and more toxic than phenolphthalein, it conducts itself in the animal organism in much the same manner as the latter compound, in that it probably combines with some substance in the cell, forming as the result of this union a compound which is hydrolyzable by hydrochloric acid.

O-CRESOLSULPHONPHTHALEIN.

On October 20, 1905, at 10.15 a. m., 0.0764 gram of o-cresolsulphonphthalein was mixed with water and the mixture injected into the peritoneal cavity of a guinea pig weighing 400 grams. At 10.20 a. m., same day, the animal passed urine which gave no coloration either with sodium hydroxide alone or after boiling with hydrochloric acid. At 1.30 p. m., same date, the animal passed urine having a deep purplish-red color. With hydrochloric acid this changed to a dark

salmon pink, and on the addition of sodium hydroxide to deep purplish red. The urine of the pig which had received the o-cresolsulphonphthalein differed from that which had received the phenolphthalein in this, that during the period of observation it always contained considerable amounts of the unaltered phthalein, whereas the urine of the pig which had received the phenolphthalein contained at most only faint traces of the phthalein and frequently none at all. On account of this fact it was difficult to determine whether any o-cresolsulphonphthalein had entered into combination in the organism. It should be noted in this connection, however, that after boiling with hydrochloric acid any given specimen of the urine of this animal gave a deeper red coloration on the addition of sodium hydroxide than did that portion of the specimen which had not been previously boiled with the acid.

SULPHONFLUORESCEIN.

On October 18, at 3.30 p. m., 0.0500 gram of sulphonfluorescein, mixed with water, was injected into the peritoneal cavity of a guinea pig weighing 335 grams. At 4.30 p. m., same date, the pupils of the eyes of this pig when examined in a strong light showed a slight greenish fluorescence. The urine of this pig, passed between 7.30 p. m. October 18 and 9 a. m. October 19, was strongly fluorescent and salmon-pink in color by transmitted light. On boiling some of the urine with dilute hydrochloric acid and adding sodium hydroxide a stronger fluorescence was noticeable than ever obtained with the urine and sodium hydroxide alone, indicating that some of the compound had probably entered into combination while in the organism.

It would seem reasonable, therefore, to conclude from these results that in the animal organism phenolphthalein and other phthaleins to a less extent enter into combination with some other substance, probably a normal constituent of the cell, to form a complex derivative, which gives no color with alkali, but which is decomposed by boiling with dilute hydrochloric acid, yielding the phthalein itself as one of the products of decomposition. In other words, it seems likely that, under these conditions, phenolphthalein forms a conjugation product, probably analogous to certain glycuronates or ethereal sulphates. On account of the extreme slowness, however, with which it is eliminated from the organism when administered in the manner above described it has been found difficult to isolate the phenolphthalein compound in question. Such being the case, the following additional observations on the conduct of the substance occurring in the urine of guinea pigs that have received phenolphthalein are not without interest, and certainly point strongly to the notion that the phenolphthalein compound is a conjugated derivative.

Solubility in organic solvents.—Some of the urine containing the phenolphthalein compound was evaporated to dryness on the water

bath and the residue extracted with absolute alcohol. The alcoholic extract was then evaporated to dryness on the water bath or until the alcohol was removed. A brownish sirup was thus obtained, which, on cooling, solidified to a mass of crystalline scales or plates. Some of these were dissolved in water and a portion of the solution made alkaline with sodium hydroxide. Only a very slight change of color was observable. Two portions of the solution of 1 cc. each were treated with dilute hydrochloric acid. One of these was boiled for five minutes, the other just brought to the boiling point and then cooled. Both were then made alkaline with sodium hydroxide. The former became deep purplish red, the latter light red. This observation goes to show that the phenolphthalein compound in the urine is soluble in absolute alcohol and also that its decomposition by hydrochloric acid is of the nature of an hydrolysis, inasmuch as it is not an instantaneous but a gradual process. Unfortunately, however, absolute alcohol dissolves other substances from the residue of the urine besides the compound in question, and the same thing has been found to be true of acetone and certain other organic solvents.

Hydrolysis by acids.—Secondly, it has been found that the extent to which the compound of phenolphthalein in the urine is decomposed or hydrolyzed by acids depends on the affinity or strength of the acid.

That such is a fact may be seen from the following: Three tubes were prepared, each containing 1 cc. of a fresh specimen of urine containing the phenolphthalein compound. To (1) was added 2 cc. of 2N hydrochloric acid, to (2), 2 cc. of 2N sulphuric, and to (3), 2 cc. of 2N acetic acid. These tubes were then heated for ten minutes on the water bath at 100° C., at the end of which time an excess of 2N sodium hydroxide was added to each tube, when the following changes of color were observed:

- (1) Dark red.
- (2) Light red.
- (3) Colorless.

Thirdly, the phenolphthalein compound is not readily decomposed or hydrolyzed even by powerful acids in the cold. That such is the case is evident from the following:

- (1) Contained 1 cc. of urine, containing the phenolphthalein compound and 2 cc. of water.
- (2) Contained 1 cc. of urine, same specimen as employed in (1), 1 cc. of water, and 1 cc. of 2N hydrochloric acid.
- (3) Contained 1 cc. of urine, same as employed in (1) and (2), and 2 cc. of 2N hydrochloric acid.

These tubes were kept at room temperature for one hour, at the end of which time a slight excess of sodium hydroxide was added to each. Tubes (1) and (2) were found to remain colorless after the addition of the sodium hydroxide. Tube (3) showed a faint trace of pink color.

Two cc. of 2N hydrochloric acid was then added to tube (2), after which it was heated to boiling for a few minutes. The tube was then cooled, and the contents made alkaline with sodium hydroxide, when the characteristic red coloration of phenolphthalein was obtained.

Action of bacteria.—As already pointed out in the above, the fresh urine of the guinea pig that had received the phenolphthalein intraperitoneally had the same color as the normal urine of the animal, varying from colorless to a decided yellow. When preserved under toluene several specimens of this urine retained their normal color. When kept without toluene, however, they gradually took on the purplish-red color characteristic of phenolphthalein in alkaline solution.

That the development of the red color of this urine on standing is really due to the action of micro-organisms is evident from the following observation:

On October 31 two tubes, (1) and (2), were prepared, each containing 5 cc. of the fresh urine of the pig that had received phenolphthalein. Both tubes were plugged with cotton wool and (2) was boiled for several minutes. Both tubes were then allowed to stand at ordinary temperature. On November 2 the contents of the tube (1) were found to have the red color characteristic of phenolphthalein, whereas the contents of tube (2) were colorless. On November 6 the red color of (1) had greatly increased in depth, whereas (2) still remained colorless.

It is evident from the results of these observations that the bacteria normally present in the urine of the guinea pig have the power of decomposing the compound of phenolphthalein present in the urine. That the difference here observable in the color of the two tubes is not due simply to an increase in the alkalinity of the urine is shown by the fact that the phenolphthalein compound present in the urine is not hydrolyzed even by strong alkali.

Action of ferments.—The fact that the phenolphthalein compound produced in the animal organism can be hydrolyzed by certain bacteria suggested that possibly it could also be hydrolyzed by the unorganized ferments. Up to the present only a few observations bearing on this point have been made. These are as follows:

One cc. of the fresh urine containing the phenolphthalein compound was mixed with 5 cc. of a clear lipolytic extract of the liver of a guinea pig, prepared according to the methods previously described by Kastle, Johnston, and Elvove,^a and the mixture kept at 40° C. for four hours. It was then made alkaline with sodium hydroxide. No pink or red coloration was observable. This experiment was repeated, using the fresh aqueous extract of the liver of the guinea pig with like negative results. Apparently, therefore, the ferments of the liver can not effect the hydrolysis of the compound of phenolphthalein produced in

^a Am. Chem. Jour., XXXI, p. 525.

the animal organism, and yet, as was proved in connection with these experiments, the substances present in the liver in no way interfere with the hydrolysis of the compound by hot hydrochloric acid.

The action of the saliva on the phenolphthalein compound of the urine was also tried. Two cc. of the fresh urine containing the phenolphthalein compound were mixed with 5 cc. of human saliva and a small amount of toluene added as a preservative. This mixture was then allowed to stand for 24 hours. At the end of this time, sodium hydroxide was then added in slight excess, when the solution took on a decided but faint pink coloration. It would seem, therefore, that saliva has the power of hydrolyzing the compound of phenolphthalein, at least to a slight extent. It is my intention to continue this investigation, in the hope of being able to obtain this phenolphthalein compound in a condition of purity, with the view of determining its composition and of more carefully studying its conduct toward acids, micro-organisms, and ferments.

A TEST FOR SACCHARIN, AND A SIMPLE METHOD OF DISTINGUISHING BETWEEN CUMARIN AND VANILLIN.

For the recognition of saccharin chemists are dependent upon its sweet taste and on the conversion of the compound into salicylic acid by heating with caustic soda.

Some time ago, while engaged in studying the color of certain of the sulphonphthaleins in acid solution, it occurred to me that possibly these compounds could be synthesized directly from saccharin without the previous conversion of this compound into o-sulphobenzoic anhydride.

In order to test the correctness of this idea, small amounts of saccharin were heated with phenol and concentrated sulphuric acid. When heated with phenol alone to the boiling point of the latter, no change is observable. On the other hand, if a small amount of sulphuric acid is present, the mass takes on a dark purplish-red color altogether similar to that obtained when phthalic anhydride, phenol, and sulphuric acid are heated in the preparation of phenolphthalein. On dissolving the melt in cold water a yellow solution was obtained, and on adding caustic soda the solution became deep purplish-red in color. Similarly, when small amounts of saccharin, resorcin, and sulphuric acid are heated together to 170°C ., the mass becomes deep orange yellow in color, and on solution in water and addition of alkali, the solution exhibits a strong greenish fluorescence, and by transmitted light exhibits the salmon pink color characteristic of sulphonfluorescein. While the opportunity has not yet presented itself for the preparation of these compounds on a large scale by this method nor for their more careful examination, there is no doubt in my own mind that these substances are sulphonphthaleins; and in this connection it occurred to me that possibly this reaction could be turned to account in the detection of minute quantities of saccharin.

The reagent employed in carrying out the tests for saccharin given in the following consists of a mixture containing 5 cc. of phenol and 3 cc. of pure concentrated sulphuric acid. When small quantities of saccharin are heated with small amounts of this reagent to 160° – 170°C . for five minutes, and the mass dissolved in a small amount of water and rendered alkaline with 2N sodium hydroxide, the solution becomes dark purplish red or pink, depending on the amount of saccharin originally taken. Any great excess of the reagent is to be avoided,

and the best results are obtained by intimately mixing the very small amounts of saccharin employed in the tests with the smallest amount of the reagent that can be got on the tip of a small glass rod by just touching the glass rod to the surface of the reagent. In order to arrive at some exact notion respecting the delicacy of the reaction the following tests were carried out, with the following results:

An aqueous solution of Merck's saccharin was prepared containing 0.5 milligram of saccharin in each cubic centimeter. In order to determine the delicacy of the reaction, known amounts of this solution were evaporated to dryness in a small porcelain dish. To the residue small amounts of the reagent were added in the manner indicated above. This was then thoroughly stirred into the residue by means of a glass rod, and the dish with its contents was then put in an air oven heated to 150° – 170° C. and allowed to remain therein for five or ten minutes. When heated for this length of time at this temperature the mixture takes on a purplish-red color if saccharin be present. After heating the desired length of time, the dish was removed from the oven and allowed to cool and water added. The results obtained with various amounts of the standard solution of saccharin are given in the following table:

Cubic centimeters of saccharin solution used.	Quantity of saccharin present, in milligrams.	Color with alkali.
0.5	0.25	Dark purplish-red.
.2	.10	Decided purplish-pink.
.1	.05	Distinctly pink.
.05	.025	Do.

This last test was repeated three times with the same result. In testing for such minute quantities of saccharin, however, care should be taken to use only very small amounts of the reagent. It will also be found advantageous with these very small amounts to keep the temperature between 145° – 160° C.

It should be borne in mind, of course, that orthophthalic acid and its derivatives, and also orthosulphobenzoic acid and its derivatives other than saccharin, would yield colored compounds with this reagent. This, however, is of no consequence, inasmuch as none of these are used in the preparation and preservation of food stuffs, and, furthermore, these compounds differ from saccharin in not having a sweet taste, so that, taking into consideration the facts as we know them, it narrowed itself down to determine whether such substances as benzoic and salicylic acids give a color by heating with this reagent, which might be confused with that obtained with saccharin. The conduct of these acids toward the reagent here employed was tested in the manner

above described, with the result that both of them gave only slightly yellowish solutions after heating with the reagent and the addition of caustic soda. In this connection it was also found that even when mixed with saccharin they in no way interfered with the delicacy of the test as ordinarily carried out. Similarly it was found that neither cumarin nor ethyl parasulphobenzoate gave any color test with the reagent.

CONDUCT OF VANILLIN TOWARD PHENOL AND SULPHURIC ACID.

A consideration of the possible substances which might occur together with saccharin in certain food stuffs and other preparations led to the thought that possibly vanillin might under some circumstances be present along with saccharin in certain preparations, the one as a flavoring, the other as a sweetening agent.

It therefore occurred to me to test the conduct of vanillin toward the reagent. It was found that when a minute quantity of vanillin is mixed with the reagent, it begins to turn yellow and then red even in the cold, and when kept at 160° – 170° C. for five minutes, the mass first becomes blood red in color and finally almost black. If the mass be then dissolved in water and a few drops 2N sodium hydroxide added, the solution becomes deep purplish red in color.

This in itself is an exceedingly delicate reaction for vanillin and is one which at first glance might be thought to seriously interfere with the use of phenol and sulphuric acid as a reagent for saccharin. However, it is a very easy matter to distinguish between saccharin and vanillin by means of this reagent on account of the marked difference in the conduct of the two substances toward it at certain temperatures. As indicated in the above, the reagent begins to act on vanillin even in the cold, whereas it has no action on saccharin even at 100° C. Advantage is therefore taken of this fact in distinguishing between vanillin and saccharin. That it is a very simple matter to distinguish between the two in this manner may be seen from the following:

Minute quantities of vanillin and saccharin, respectively, were mixed with a small amount of the reagent and heated for five minutes in a bath of boiling water. The mass containing the vanillin became blood red in color under these conditions, and on the addition of water it gave a pink, somewhat turbid, solution which, on the addition of a few drops of 2N sodium hydroxide, became clear and deep purplish-red in color. On the other hand, the mass containing the saccharin remained colorless, and with water and alkali gave a perfectly clear, colorless solution. In spite of the fact, therefore, that both of these substances produce red coloring matters when heated with phenol and sulphuric acid, it is still an easy matter to distinguish between them by means of this reagent.

TO DISTINGUISH BETWEEN CUMARIN AND VANILLIN.

As is well known, the cheaper extracts of vanilla contain both vanillin and cumarin. Ordinarily these two substances are separated from vanilla extracts by Winton's^a modification of the Hess-Prescott^b method and their identity established by difference in the melting point, vanillin melting at 80°–81° C. and cumarin at 67° C. Leach^c has also found that vanillin and cumarin when crystallized from ether show differences with crossed nicols, vanillin giving marked color, but cumarin giving none.

Vanillin also gives a more marked color with sodium nitrite and sulphanilic acid, but, as pointed out by Leffman and Beam,^d this reaction is not characteristic.

By means of the reagent here recommended for saccharin, it becomes a very easy matter to distinguish between these two substances. As already pointed out, cumarin yields no coloring matter when heated with phenol and sulphuric acid, even at 160° to 170° C., whereas vanillin yields a beautiful red coloring matter, the reaction taking place rapidly at 100° C., and to some extent even at ordinary temperatures. That such is the case may be seen from the following observations:

Minute quantities of cumarin and vanillin, respectively, were mixed with small amounts of the reagent and heated for five minutes in a bath of boiling water. Under these conditions the cumarin gave a colorless melt, whereas the vanillin gave a blood-red one. On adding water and a few drops of 2N sodium hydroxide to the tube containing the cumarin no change of color occurred, whereas with water and alkali the mixture which originally contained the vanillin became dark purplish red.

It has been found that other phenols give characteristic color reactions both with saccharin and vanillin. That such is the case may be seen from the following:

Small amounts of saccharin were mixed with small quantities of the phenols named in the table, together with small amounts of sulphuric acid, and heated to 160° to 170° C. for five minutes. The product obtained in each case was then dissolved in water and a few drops of 2N sodium hydroxide added, with the following results:

Name of phenol.	Color with alkali.
Pyrocatechin	Green.
Hydroquinone	Purplish brown, blue fluorescence.
Resorcin	Salmon pink, strong, greenish-yellow fluorescence.
Trikresol ^e	Purplish red.
Phloroglucin	Wine red.
Thymol	Light blue.

^aJour. Am. Chem. Soc. 1902. 1129.

^bIbid., 1899, 257.

^cFood Analysis, Leffman and Beam, 2d ed., p. 324.

^dIbid., p. 324.

^eTrikresol is the trade name of an antiseptic mixture containing the three cresols in nearly equal quantities.

With vanillin, at 100° C., the following results were obtained:

Name of phenol.	Color with alkali.
Pyrocatechin.	Dark blue to green.
Hydroquinone	Purplish brown.
Resorcin	Red, with slight greenish fluorescence.
Trikresol	Deep purplish red.
Phloroglucin.....	Yellow.
Thymol	Light red.

With cumarin, at 100° C., concentrated sulphuric acid and the above-named phenols gave no highly colored compounds, the color varying from orange yellow in the case of phloroglucin to colorless in the case of trikresol.

Control experiments were also tried in which these several phenols alone were heated with concentrated sulphuric acid to 160°–170° C. for five minutes. On dissolving in water and making alkaline with sodium hydroxide they gave colorless or slightly yellow solutions. The control with resorcin gave a slight greenish fluorescence on the addition of the alkali. This might have been due to impurities in this particular specimen of the compound. However, it is not sufficient to introduce any error or confusion into the results herein set forth.

Aside from its utility in the tests herein described the fact that saccharin and vanillin yield dyestuffs so readily is a matter of considerable chemical interest in itself. Further investigations along these lines will be carried out with the view of determining how advantageously saccharin can be employed in the synthesis of the sulphon-phthaleins, and with the view of determining the composition and nature of these vanillin dyes, which, so far as I am aware, have never been described.

THE TOXICITY OF OZONE AND OTHER OXIDIZING AGENTS TO LIPASE.

My attention was directed to the general subject of the toxicity of ozone through a few observations that were made in my laboratory on the odor of this substance. On being asked to describe the odor of small amounts of ozone, two out of six persons, not chemists, described it as similar to that of hydrocyanic acid. Considering the great difference in the chemical composition of the two substances, this in itself is interesting, and at once suggested the idea that possibly ozone, like hydrocyanic acid, might be a protoplasmic poison. In fact, it is known to be an irritant poison to higher animals. It is also toxic to microorganisms, and recently it has been shown by Sigmund^a to be poisonous to a number of unorganized ferments, such as invertase, pepsin, emulsin, etc. It therefore occurred to me that it might prove of interest to test its toxicity toward lipase, inasmuch as but few substances except hydrofluoric acid and the fluorides exert any powerfully toxic action on this ferment, particularly on that obtained from the liver of the hog.

The ozone used in these experiments was obtained by the electrolysis of water containing sulphuric acid. The gas liberated at the anode during the electrolysis was collected in a series of 50 cc. measuring flasks, and the amount of ozone determined in the first and last flasks of a series by passing the gas through a solution of potassium iodide and titrating with N/50 sodium thiosulphate. The ozone in 50 cc. of the gas first employed in these experiments liberated an amount of iodine equivalent to 0.65 cc. of N/50 sodium thiosulphate. This is equivalent to 0.312 milligram of ozone in 50 cc. or 6.24 milligrams of ozone per liter.

The effect of this amount of ozone on a clear solution of hog liver lipase, prepared according to the method described by Kastle, Johnston, and Elvove,^b was tested in the following manner:

Five cubic centimeters of the clear lipase solution was introduced into each of two glass-stoppered flasks; one of these, No. 1, contained 0.312 milligram of ozone; the other, No. 2, was filled with atmospheric air. The flasks were then closed and sealed with paraffin and kept in a dark closet, at ordinary temperature, for twenty-four hours. At the end of this time the odor of the ozone had entirely disappeared from

^aCentr. Blatt. f. Bact. (2) Bd. XIV, Nos. 12, 13.

^bAm. Chem. Jour. XXXI, p. 525.

the flask originally containing it, and the clear lipase solution had altered considerably in appearance. It now contained quite a perceptible coagulum, whereas that in the flask containing air still remained clear. The lipolytic activity of the two solutions was then tested by adding to each 10 cc. of a N/20 solution of ethyl butyrate; 10 cc. of such a solution, if completely hydrolyzed, would require 5 cc. of N 10 sodium hydroxide to neutralize the butyric acid formed. A drop of an alcoholic solution of phenolphthalein was also added to each flask, and the free acid in each neutralized with N 10 sodium hydroxide. The two flasks were then allowed to stand at ordinary temperature, and the amount of hydrolysis in each determined from time to time by means of N 10 sodium hydroxide, with the following results:

Time.	Cubic centimeters N 10 sodium hy- droxide required.		Per cent of hydrol- ysis.	
	No. 1.	No. 2.	No. 1.	No. 2.
$\frac{1}{2}$ hour	None.	0.45	0	9
1 hour	None.	.45	0	9
2 hours	None.	.90	0	18
24 hours	0.10	3.30	2	66
Total10	5.10	2	102

It is evident, therefore, from these results that a solution of clear lipase, 5 cc. of which can ordinarily hydrolyze 0.058 gram of ethyl butyrate in twenty-four hours, under the conditions given in the above will, after it has been acted upon by 0.312 milligram of ozone, hydrolyze only 0.00116 gram of ethyl butyrate.

A second lot of ozonized oxygen was prepared, 50 cc. of which was found to liberate an amount of iodine equivalent to 2.2 cc. N 50 sodium thiosulphate. From this it follows that the gas contains 1.009 milligrams of ozone in 50 cc. In order to test the toxicity of ozone of this concentration to lipase, 5 cc. of a clear lipase solution were introduced into a glass-stoppered flask, No. 1, containing this amount of ozone, and 5 cc. of the lipase solution into a flask of the same capacity, No. 2, filled with air. The two flasks were allowed to stand in a dark closet forty minutes, at ordinary temperature. After exposure to the ozone for this interval, the lipase solution, which was perfectly clear and transparent originally, was found to have become cloudy and more or less opaque, and the odor of ozone had largely disappeared from the flask. Ten cc. of a N/20 solution of ethyl butyrate were then added to each flask, also a drop of phenolphthalein, and the solutions rendered neutral by means of N 10 sodium hydroxide. The flasks were then allowed to stand at ordinary temperature and the amount of

hydrolysis determined from time to time by means of N/10 sodium hydroxide solution, with the following results:

Time.	Cubic centimeters N/10 sodium hy- droxide required.		Per cent of hydrol- ysis.	
	No. 1.	No. 2.	No. 1.	No. 2.
$\frac{1}{2}$ hour.....	None.	1.00	0	20
1 hour and 10 minutes.....	None.	1.50	0	30
4 hours and 15 minutes.....	0.05	2.50	1	50
Total	0.05	5.00	1	100

It is evident, therefore, from these results that an amount of lipase capable of hydrolyzing 0.0580 gram of ethyl butyrate in five hours and fifty-five minutes is practically destroyed when exposed to the action of 1.009 milligrams of ozone for forty minutes.

COMPARISON OF OTHER OXIDIZING AGENTS AND ANTISEPTICS WITH OZONE.

In the light of these results, it seemed of interest to compare various other oxidizing agents and antiseptics with ozone with regard to their toxicity to lipase. Thus far 16 substances have been tested. These are: Chlorine, bromine, iodic acid, chromic acid, perosmic acid, succinic peroxide acid, hydrocyanic acid, iodine cyanide, sodium fluoride, formic aldehyde, trikresol,^a silver nitrate, copper sulphate, mercuric chloride, potassium permanganate, and potassium nitrite.

Solutions of these several substances were prepared of such concentration that 1 cc. of a given solution contained a quantity of the substance equivalent to 0.312 milligram of ozone, or with such of these as are oxidizing agents, 1 cc. of a given solution contained a quantity of the substance capable of furnishing an amount of oxygen equivalent to the active oxygen in 0.312 milligram of ozone.

In order to test the toxicity of these several substances to lipase, 1 cc. of the solution of the substance was added to a clear solution of liver lipase of the hog and the mixture allowed to stand at ordinary temperature twenty-four hours; 10 cc. of N/20 ethyl butyrate were then added and the mixture again allowed to stand in the dark for twenty-four hours. The acid resulting from the hydrolysis of the ethyl butyrate by lipase was then titrated with N/10 sodium hydroxide. The normal lipolytic power of the lipase solution employed in this series of experiments was determined in the following manner: 1 cc. of water was added to 5 cc. of the lipase solution and the mixture allowed to stand twenty-four hours at ordinary temperature in the dark; 10 cc.

^a Trikresol is the trade name of a mixture of the three cresols.

of N/20 ethyl butyrate were then added and the mixture allowed to stand also for twenty-four hours at ordinary temperature in the dark. At the end of this time the acid resulting from the hydrolysis was titrated with N/10 sodium hydroxide. The results of these experiments, together with the names of the substances employed and the several amounts in milligrams in which they were used, are given in the following table:

Name of substance.	Amount used in milligrams.	Cubic centi- meters of N/10 sodium hydroxide required.	Per cent of hydrolysis.
Water.....	None.	3.07	61.40
Iodic acid.....	0.384	2.80	56.00
Silver nitrate.....	1.1045	3.11	62.20
Mercuric chloride.....	3.521	1.89	37.80
Chromic acid.....	.217	2.30	46.00
Perosmic acid.....	.4143	1.62	32.20
Potassium permanganate.....	.4112	.92	18.40
Copper sulphate.....	3.2455	2.31	46.20
Potassium nitrite.....	1.1070	3.03	60.60
Iodine cyanide.....	.9945	.70	14.00
Succinic acid.....	.7670	3.00	60.00
Succinic acid peroxide.....	1.5210	.35	7.00
Formic aldehyde.....	.1950	3.07	61.40
Hydrocyanic acid.....	.1755	2.91	58.20
Trikresol.....	.7020	2.95	59.00
Sodium fluoride.....	.5470	.06	1.20
Chlorine.....	.4608	0	0
Bromine.....	1.04	.10	2.00

It is clear from these results that so far as their toxicity or non-toxicity to lipase is concerned under the conditions indicated these substances fall into several distinct groups. First, those which are practically nontoxic, including silver nitrate, iodic acid, formic aldehyde, the cresols, hydrocyanic acid, potassium nitrite, and succinic acid. Secondly, those that are moderately toxic, including mercuric chloride, chromic acid, copper sulphate, and perosmic acid. Thirdly, those that are powerfully toxic, including ozone, chlorine, bromine, sodium fluoride, succinic peroxide acid, iodine cyanide, and potassium permanganate. It is interesting to note that the first two groups contain a number of substances highly toxic to many living forms, whereas, with one exception, the last group is composed of powerful oxidizing agents.

TOXICITY AND TEMPERATURE.

It has also been observed that the toxicity of iodine cyanide to lipase is increased by rise of temperature. That such is the case is evident from the following results:

Two series of experiments with this substance were carried out, one at 10° C. and the other at 40° C., in which 1 cc. of water, or 1 cc. of an

aqueous solution of iodine cyanide containing 0.9945 milligram of the substance, was allowed to act on 5 cc. of a clear solution of lipase for 24 hours at the above-named temperatures, the experiments being carried on in glass-stoppered flasks. At the end of this time, 10 cc. of N/20 ethyl butyrate were added to each flask. These were then allowed to stand 24 hours at ordinary temperature and were then titrated with N/10 sodium hydroxide, with the following results:

TEMPERATURE, 10° C.

Name of substance.	Cubic centimeters of sodium hydroxide required.	Per cent of hydrolysis.
Water (control)	3.65	73
Iodine cyanide80	16
Do75	15

TEMPERATURE, 40° C.

Water (control)	2.90	58
Iodine cyanide00	0
Do05	1

It is evident, therefore, from these results, that at 40° C. the ferment is completely destroyed by this amount of iodine cyanide, whereas at 10° C., with the same amount of iodine cyanide, it retains more than one-fifth of its original activity.

THE INFLUENCE OF CHEMICAL CONSTITUTION ON THE LIPOLYTIC HYDROLYSIS OF ETHEREAL SALTS.

Several years ago it was shown by Loevenhart and myself^a that active extracts of the pancreas and liver of the hog have the power of hydrolyzing various ethereal salts. In this connection it occurred to us to undertake a comparative study of the hydrolysis of various ethereal salts by lipase with the view of determining, if possible, the influence of their chemical constitution on the rate of the lipolytic hydrolysis. On account of the lack of material in the way of pure esters, however, and for other reasons, it was possible at the time to make only a few observations on the rate of hydrolysis of the ethyl esters of formic, acetic, propionic, and butyric acids. These, however, were sufficient to indicate that, leaving ethyl formate out of consideration, the rate of hydrolysis of ethereal salts by both pancreatic and hepatic lipase increases with increase in molecular weight of the ethereal salt and with increase in molecular complexity of the acid radical thereof. As originally carried out, however, our experiments were open to the objection that neither the ferment nor the ethereal salt was entirely in solution.

With the view of remedying this experimental defect in the method, these experiments have been repeated, using perfectly clear solutions of liver lipase and aqueous solutions of the ethereal salts containing equivalent quantities of the various esters employed. The very sparing solubility of many of the ethereal salts in water has rendered it necessary to work with very dilute solutions of these substances, thereby greatly increasing the possibility of experimental error. Up to this time this has been the chief experimental difficulty encountered, but it is by no means the only one. The results herein presented are therefore given tentatively in the hope that the method of investigation may be still further improved upon. With the exception of the work of Fischer,^b Armstrong,^c and others on the selective action of certain enzymes on certain glucosides, and of the work of Fischer and Abderhalden^d on the conduct of various polypeptides toward the pancreatic ferment, these results are of interest as being the first attempt

^a Am. Chem. Jour. XXIV, 491-525.

^b Berichte der deutschen chemischen Gesellschaft, 1894, pp. 1429, 2071, 2985, 3479.

^c Proc. Physiol. Soc., 1905, iv; J. Physiol., 33.

^d Sitzungsber. K. Akad. Wiss. Berlin, 1905, 290-300.

to determine with any degree of accuracy the influence of chemical constitution on those changes which can be brought about by means of the unorganized ferments.

It should be observed in this connection that these observations have not been made consecutively, but from time to time whenever the material could be obtained. It has therefore been impracticable to make use of the same specimen of lipase throughout the investigation. This, together with the fact that the experiments were carried out at ordinary temperature, which of course varies within narrow limits from day to day, accounts for the fact that the same amount of a given ethereal salt has not always been hydrolyzed by the same volume of clear lipase during equal intervals. In every series of experiments, however, some of the more common ethereal salts, such as methyl or ethyl acetate, or ethyl butyrate, have been included, in order to afford the proper basis of comparison.

THE EFFECT OF THE ALKYL RADICAL ON THE LIPOLYTIC HYDROLYSIS OF ETHEREAL SALTS.

In order to determine the effect of certain alkyl radicals on the lipolytic hydrolysis of various ethereal salts, the following experiments were tried:

Fifty cubic centimeters of N/100 aqueous solutions of the ethereal salts named in Table I were brought together with 5 cc. of a clear solution of liver lipase and the mixture allowed to stand at ordinary temperature for a certain length of time, usually one hour. The solutions were then titrated with N/10 sodium hydroxide, with the following results:

TABLE I.

No. of series.	No. of experiment.	Name of ester.	Time.	Cubic centimeters N/10 sodium hydroxide required.	Per cent of hydrolysis.
1	1	Methyl formate	1 hour.....	0.80	16.0
	2	Ethyl formate.....	do87	17.4
2	3	Methyl formate	do50	10.0
	4	Ethyl formate.....	do60	12.0
3	5	Methyl acetate	do50	10.0
	6	Ethyl acetate	do40	8.0
	7	Allyl acetate	do55	11.0
4	8	Methyl acetate	2½ hours...	.85	17.0
	9	Ethyl acetate	do90	18.0
	10	Benzyl acetate	do	1.00	20.0
5	11	Methyl acetate	15 hours...	2.00	40.0
	12	Ethyl acetate	do	2.45	49.0
	13	Methyl propionate	do	3.35	67.0
6	14	Ethyl propionate.....	do	3.95	79.0
	15	Methyl butyrate.....	1 hour.....	1.10	22.0
	16	Ethyl butyrate.....	do	1.30	26.0
7	17	Methyl benzoate	do35	7.0
	18	Ethyl benzoate.....	do45	9.0

The hydrolysis of ethyl, normal butyl, and iso-butyl acetates by lipase has been determined under the following conditions: 10 cc. of the N/40 solutions of these esters were brought together with 5 cc. of a clear solution of liver lipase. One set of experiments was allowed to stand for one hour, the other for four hours, when they were titrated with N/50 sodium hydroxide, with the following results:

TABLE 2.

No. of series.	No. of experiment.	Name of ester.	Time.	Cubic centimeters N/50 sodium hydroxide required.	Per cent of hydrolysis.
8	19	Ethyl acetate	1 hour.....	0.60	4.8
	20	Butyl acetatedo50	4.0
	21	Iso-butyl acetatedo55	4.4
9	22	Ethyl acetate	4 hours....	1.10	8.8
	23	Butyl acetatedo80	6.4
	24	Iso-butyl acetatedo80	6.4

These results furnish us with the following coefficients whereby to express the effect of the several alkyl radicals on the lipolytic hydrolysis of ethereal salts in terms of the methyl and ethyl radicals as unity.

Name of radical.		Lipolytic coefficients in terms of methyl as unity.
Ethyl, from experiments	{ 1 and 2	1.08
	{ 3 and 4	1.2
	{ 5 and 6	.8
	{ 8 and 9	1.06
	{ 11 and 12	1.225
	{ 13 and 14	1.18
	{ 15 and 16	1.18
	{ 17 and 18	1.28
Mean		1.128
Allyl, from experiments.....	5 and 7	1.10
Benzyl, from experiments	8 and 10	1.17
		In terms of ethyl as unity.
Butyl, from experiments	{19 and 20	.84
	{22 and 23	.73
Iso-butyl, from experiments	{19 and 21	.91
	{22 and 24	.73

These numbers indicate that the alkyls, methyl, ethyl, butyl, isobutyl, allyl, and benzyl exert very nearly the same influence on the hydrolysis of an ethereal salt by lipase; the greatest difference observable being an increase of ethyl over methyl of 0.28, in terms of methyl as unity, and a decrease of butyl and iso-butyl as compared with ethyl of about one-fourth, in terms of ethyl as unity. The fact that butyl and iso-butyl acetate are hydrolyzed to practically the same

extent by lipase is of interest as indicating that the structural difference between these radicals is without influence on the lypolytic process.

THE EFFECT OF THE ACID RADICAL ON THE LIPOLYTIC HYDROLYSIS OF ETHEREAL SALTS.

In order to determine the effect of the acid radical of the ethereal salt on the rate of the hydrolysis of these compounds by lipase, the following experiments were carried out:

Three solutions were prepared (1) containing 50 cc. N/100 methyl acetate, (2) 50 cc. N/100 methyl propionate, and (3) 50 cc. of N/100 methyl butyrate. Five cubic centimeters of a clear solution of lipase was added to each of these solutions, and after standing for one hour at ordinary temperature they were titrated with N/10 sodium hydroxide. The following results were obtained:

Name of ester.	Cubic centimeters N/10 sodium hydroxide required.	Per cent of hydrolysis.
Methyl acetate	0.10	2
Methyl propionate.....	.45	9
Methyl butyrate.....	.95	19

In a second series of experiments the conditions being the same as in the first, except that a different solution of lipase was employed, the following numbers were obtained:

Name of ester.	Cubic centimeters N/10 sodium hydroxide required.	Per cent of hydrolysis.
Methyl acetate	0.30	6
Methyl propionate.....	.60	12
Methyl butyrate.....	1.10	22

A third series gave the following results:

Name of ester.	Cubic centimeters N/10 sodium hydroxide required.	Per cent of hydrolysis.
Methyl acetate	0.10	2
Methyl propionate.....	.40	8
Methyl butyrate.....	.75	15

Similar experiments were tried using the ethyl esters of these three acids, the other conditions of the experiments remaining the same.

The results are as follows:

Name of ester.	Cubic centimeters N/10 sodium hydroxide required.	Per cent of hydrolysis.
Ethyl acetate.....	0.05	1.00
Ethyl propionate.....	.60	12.00
Ethyl butyrate.....	1.10	22.00

In a second series of experiments with the ethyl esters, in which the lipase was allowed to act for two hours, the other conditions being the same as those given above, the following numbers were obtained:

Name of ester.	Cubic centimeters N/10 sodium hydroxide required.	Per cent of hydrolysis.
Ethyl acetate.....	0.45	9.00
Ethyl propionate.....	1.70	34.00
Ethyl butyrate.....	2.80	56.00

It will be observed that both with the methyl and ethyl esters of these acids, the general trend of the results is the same, and that the same relation holds for the two series of ethereal salts. It is also evident from these results that unlike the alkyl radical, the acid radical in an homologous series of ethereal salts exerts a great influence on their hydrolysis by lipase. It will be seen that the amount of propionate hydrolyzed in a given time by lipase is almost an exact mean between the several amounts of acetate and butyrate hydrolyzed during the same interval under the same conditions of temperature, etc. In view of the chemical relation existing between these three substances this is an interesting fact, and tends to confirm the earlier results obtained by Loevenhart and myself with pancreatic lipase.

Some determinations have also been made of the rate of hydrolysis of methyl and ethyl formates as compared with the corresponding acetates under the following conditions: Four solutions were prepared containing 50 cc. of N/100 methyl and ethyl formate and methyl and ethyl acetate, respectively. To each of these 5 cc. of a clear solution of lipase was added. They were then allowed to stand at ordinary temperature for one hour, at the end of which time they were titrated with N/10 sodium hydroxide with the following results:

Name of ester.	Cubic centimeters of N/10 sodium hydroxide required.	Per cent of hydrolysis.
Methyl formate.....	0.80	16.0
Ethyl formate.....	.87	17.4
Methyl acetate.....	.60	12.0
Ethyl acetate.....	.65	13.0

It is evident, therefore, from these results that the formates are hydrolyzed slightly more rapidly by lipase than the acetates. Working with pancreatic lipase under somewhat different conditions Loevenhart and myself found ethyl formate and ethyl acetate to be hydrolyzed with equal rapidity. From the relation which has been found to hold for the acetates, propionates, and butyrates, so far as their hydrolysis by lipase is concerned, we might be led to expect that the formates would be hydrolyzed by lipase somewhat less readily than the acetates. The fact that they are not, however, is in keeping with other abnormalities displayed by formic acid and its derivatives as compared with other acids of the fatty-acid series.

ETHYL BUTYRATE AND ETHYL ISO-BUTYRATE.

The rate of hydrolysis of ethyl butyrate and ethyl iso-butyrate by lipase has also been determined under the following conditions: Solutions were prepared containing 10 cc. of N/20 ethyl butyrate and ethyl iso-butyrate, respectively, and 5 cc. of a clear solution of lipase. These solutions were then allowed to stand at ordinary temperature—20° C.—for the desired interval, at the end of which time they were titrated with N/50 sodium hydroxide with the following results:

Time.	Cubic centimeters N/50 sodium hydroxide required.		Per cent of hydrolysis.	
	Butyrate.	Iso-butyrate.	Butyrate.	Iso-butyrate.
1 hour	2.2	2.2	8.8	8.8
3 hours.....	3.65	4.90	14.6	19.6
5 hours.....	5.10	5.90	20.4	23.6

With another specimen of lipase, the other conditions being the same as in the preceding, the following results were obtained:

Time.	Cubic centimeters N/50 sodium hydroxide required.		Per cent of hydrolysis.	
	Butyrate.	Iso-butyrate.	Butyrate.	Iso-butyrate.
1 hour	1.85	1.95	7.4	7.8
3 hours.....	3.50	4.00	14.0	16.0

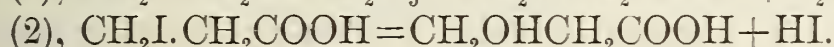
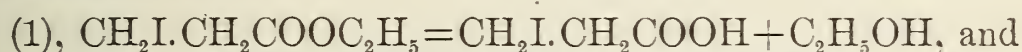
It is evident therefore that there is no marked difference in the rate of hydrolysis of these two ethereal salts by lipase.

Ethyl β -iodopropionate has been compared with ethyl acetate and ethyl butyrate in its conduct toward lipase using N/80 solutions of

these several esters. Solutions were prepared containing 10 cc. of the N/80 solution of each of these esters and 5 cc. of clear lipase. These were allowed to stand at 20° C. for one and three hours, respectively, and were then titrated with N/50 sodium hydroxide. The following results were obtained:

Time.	Cubic centimeters N/50 sodium hydroxide required.			Per cent of hydrolysis.		
	β -iodopropionate.	Acetate.	Butyrate.	β -iodopropionate.	Acetate.	Butyrate.
1 hour	1.3	0.50	1.6	20.8	8.0	25.6
3 hours.....	2.60	.65	3.05	41.6	10.4	48.8

At the time that these observations were made on the ethyl β -iodopropionate no ethyl propionate was at hand with which to compare it. It is evident, however, from these results and from what has gone before, that ethyl β -iodopropionate is readily hydrolyzed by lipase and that the introduction of an iodine atom into the β position in the molecule of ethyl propionate does not exert any retarding effect on the hydrolysis of the ester by lipase, but if anything accelerates the hydrolysis somewhat. It still remains to be determined, however, whether any secondary decomposition of the β -iodopropionic acid has occurred under these conditions, in which event two molecules of acid would result from the decomposition of one molecule of the ethyl β -iodopropionate, thus:



It is obvious that were these changes to occur simultaneously the results with ethyl β -iodopropionate given above would be too high by one-half. However, there is no great likelihood that the change represented by equation (2) would take place with measurable rapidity at this great dilution.^a

Ethyl cyanacetate has also been compared with ethyl acetate in its conduct toward lipase, using N/20 solutions of the esters. At this dilution ethyl cyanacetate is slowly hydrolyzed even by pure water. This change is a slow one, however, and in no way interferes with the study of its hydrolysis by lipase. In order to form some idea of the rapidity with which ethyl cyanacetate is hydrolyzed by lipase and with the view of comparing it with ethyl acetate in this respect two solutions were prepared, (1) containing 10 cc. N/20 ethyl cyanacetate and 5 cc. of clear lipase solution and (2) containing 10 cc. N/20 ethyl

^a See the work of Kastle and Keiser "On the Decomposition of the Salts of Monochloracetic and Monobromacetic Acids." Am. Chem. Jour., XV, 471-493, 1893.

acetate and 5 cc. of clear lipase solution. These solutions were allowed to stand at 20° C. for one and two hours, respectively, when they were titrated with N/50 sodium hydroxide, with the following results:

Time.	Cubic centimeters, N/50 sodium hydroxide required.		Per cent of hydrolysis.	
	Acetate.	Cyanacetate.	Acetate.	Cyanacetate.
1 hour	0.8	0.6	3.2	2.4
2 hours	1.05	.85	4.2	3.4

With another specimen of lipase, the other conditions of the experiment remaining the same, the following results were obtained:

Time.	Cubic centimeters, N/50 sodium hydroxide required.		Per cent of hydrolysis.	
	Acetate.	Cyanacetate.	Acetate.	Cyanacetate.
2 hours	0.95	0.65	3.8	2.6
4 hours	1.30	.70	5.2	2.8

With still another specimen of lipase, the other conditions the same as those given in the above, the following results were obtained:

Time.	Cubic centimeters, N/50 sodium hydroxide required.		Per cent of hydrolysis.	
	Acetate.	Cyanacetate.	Acetate.	Cyanacetate.
17 hours	2.10	1.00	8.4	4.0

It will be seen from these results that the introduction of a cyanogen radical into the molecule of an ethereal salt does not greatly alter its conduct toward lipase. At most, the rate of hydrolysis by lipase is diminished one-half. It seems, further, that for shorter intervals the rate of hydrolysis of these two ethereal salts by lipase are more nearly equal than they are for longer intervals. The probable explanation of this is that, so far as the esters themselves are concerned, both are probably hydrolyzed by lipase with nearly equal rapidity. The cyanacetic acid, however, being a stronger acid than acetic and probably more toxic in other respects, doubtless inhibits the activity of lipase to

a greater degree than acetic, and hence as it accumulates in the liquid the hydrolysis of the ethyl cyanacetate is correspondingly diminished.

It has been shown by Kastle, Johnston, and Elvove^a that this gradual falling off in velocity is characteristic of the lipolytic process generally, and in every instance is apparently due to the same cause, namely, the accumulation of acid in the solution and the inhibition of the ferment thereby. This fact should always be taken into account in determining the relative stability of various esters toward lipase. It will be my object in the future to determine with greater exactness the proper standards for such comparisons as these herein presented, in the hope of being able ultimately to determine the lipolytic constant of an ester with greater accuracy.

^aAm. Chem. Jour., XXXI, 534-536.

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TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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M. J. ROSENAU, Director.

APRIL 9, 1906.

THE LIMITATIONS OF FORMALDEHYDE GAS
AS A DISINFECTANT,

WITH SPECIAL REFERENCE TO CAR SANITATION.

BY

THOMAS B. McCLINTIC.



WASHINGTON:
GOVERNMENT PRINTING OFFICE.
1906.

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WALTER WYMAN, *Surgeon-General*,
United States Public Health and Marine-Hospital Service.

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THE LIMITATIONS OF FORMALDEHYDE GAS AS A DISINFECTANT, WITH SPECIAL REFERENCE TO CAR SANITATION.

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INTRODUCTION.

This work was undertaken in order to throw further light upon the much discussed question as to the merits of formaldehyde gas as a germicidal agent and the best method of obtaining it for disinfecting purposes, a problem which has been of much interest to the Service in its public health work, particularly in its relation to car sanitation.

Some preliminary experiments soon showed certain limitations to the use of formaldehyde gas as a disinfectant, and on account of the practical importance of these limitations they were taken up and studied under definite conditions.

A special study was made of the production of formaldehyde gas by the action of potassium permanganate on formalin. When these two substances are brought together a vigorous reaction takes place accompanied by rapid liberation of formaldehyde gas.

Although this is a comparatively new method of liberating the gas it is not clear, from a review of the literature, who was the first to suggest it. Certainly among the first to describe it was Dr. G. F. Johnson, of Sioux City, Iowa; this was done in a paper read at the eighth semiannual meeting of the Sioux Valley Medical Association held at Sioux City, Iowa, January 21 and 22, 1904. In the spring and summer of the same year Henry D. Evans,^b chemist, and Dr. J. P. Russell, bacteriologist, of the Laboratory of Hygiene, Augusta, Me., conducted experiments with formaldehyde gas liberated by this method;

^aAcknowledgments: To Daniel Base, Ph. D., technical assistant in pharmacology, Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service, I am indebted for the chemical determinations made during warm weather and for assistance in the preparation of the corresponding part of the text of this bulletin; and to Madison B. Porch, B. S., assistant in the division of pharmacology, Hygienic Laboratory, for assistance in making the chemical determinations during cold weather.

^b Evans, Henry D., and J. P. Russell: Formaldehyde disinfection. 13th Ann. Rep. Maine State Board of Health.

they made determinations of the percentage of gas liberated and tests of its properties as a disinfectant. Their results indicated this method of liberating the gas to be an efficient as well as an ideal one as regards simplicity and rapidity.

As the published reports of almost innumerable experiments with formaldehyde give such contradictory results, a further study of this question by us has resulted not only in explaining the reason of these contradictory results, but also has developed distinct limitations to the use of the gas as a disinfecting agent.

For comparison with the formalin-permanganate method many experiments under similar conditions were also carried out with each of the other well-known methods of obtaining formaldehyde gas, namely, the retort, autoclave, generating lamp, sheet-spraying, and formalin-aluminum sulphate-lime methods.

In order to make our comparisons complete, it was necessary to know, in addition to the relative power for destroying microorganic life, the quantity of formaldehyde gas present in the atmosphere of the room; or, in other words, the yield of gas from a definite amount of formalin by the various methods employed. A room was chosen which afforded special advantages for conducting chemical as well as bacteriological experiments. Quantitative chemical determinations of the percentage of gas liberated were made simultaneously with bactericidal tests by drawing a definite volume of air from the room through an absorbing solution and determining the amount of formaldehyde absorbed.

Our method of making the bacteriological exposures in the experiments in the room differs somewhat from those usually employed by other experimenters. The difference consists principally in having a room provided with special apparatus, so that the cultures of the different organisms can be introduced into and removed from the formaldehyde in the room and planted in bouillon whenever desired. This enabled us to ascertain almost exactly the time that a given charge of formaldehyde required to exert its germicidal action upon the different organisms exposed. By making the chemical determinations simultaneously with the bacteriological tests the quantity of formaldehyde per cubic foot of air in the room at certain stages of the experiment was ascertained. The results of a few experiments in this room showed that the formalin-permanganate method, besides being rapid and simple, compared very favorably with the retort and autoclave methods as regards the percentage of formaldehyde gas liberated and its power to destroy microorganic life.

A request was made of the local management of the Pullman Company for the use of some of their cars for experimental purposes, which was cheerfully granted. The work was taken up in railroad

cars and a number of experiments conducted with various methods of liberating the gas.

As our studies progressed it became evident that changes in climatic conditions caused a wide variation in our results. Consequently our work was continued through the different seasons of the year in order to observe the influence of temperatures, humidity, wind, etc.; but as the germicidal power of the gas during cold weather was very unsatisfactory, only a limited number of experiments were necessary during the winter season.

A number of experiments with the formalin-permanganate method were performed in large glass bottles. In this manner it was possible to control or eliminate some of the atmospheric conditions with which we had to contend in the room and cars. Particular attention was given to the influence of humidity upon the bactericidal power of formaldehyde, as well as to the percentage of formaldehyde liberated and that remaining in the residue.

Our bacteriological experiments were carried out with the purpose principally of determining the properties of formaldehyde gas as a surface disinfectant, it being taken for granted that formaldehyde possesses only slight penetrating power.

In the following pages the work is given under three headings, namely—

1. Experiments in a special room.
2. Experiments in a large bottle with the formalin-permanganate method.
3. Disinfection of sleeping cars with formaldehyde gas.

EXPERIMENTS IN A SPECIAL ROOM.

DESCRIPTION OF ROOM.

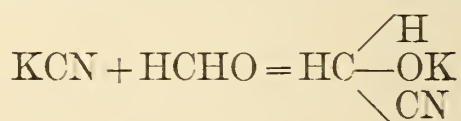
The room into which the formaldehyde gas was liberated contained 2,000 cubic feet of air space. The walls, floor, and ceiling were of ordinary tongue and groove construction, and in addition to this the room was lined throughout, except over the windows, with sheet zinc, closely nailed at the joints. There were two windows and two doors, all of which were made to fit closely. The windows were on opposite sides and the doors opened into adjoining rooms, so that the experiment room was freely exposed to the winds on two sides. While comparatively close, it was of course not air-tight.

One wall was pierced by three horizontal rows of zinc tubes about $2\frac{1}{4}$ inches in diameter, one row being about a foot from the floor, one midway between the floor and the ceiling, and one about a foot from the ceiling. Each tube was provided with a sliding wooden frame carrying a small wire tray for the purpose of making the bacteriological

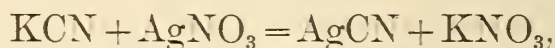
exposures. This frame was long enough so that when in position the wire tray would be entirely within the room containing the formaldehyde, the outer end of the frame being pushed just far enough into the tube through which it was introduced to close the outer opening of the tube with a tight-fitting rubber stopper. Some of these zinc tubes were also utilized for drawing air from the room in making the chemical determinations.

DETERMINATION OF THE AMOUNT OF FORMALDEHYDE IN THE ATMOSPHERE OF THE ROOM.

The quantity of formaldehyde in the atmosphere of the room during any particular experiment was determined by the potassium cyanide method of Romijn. This method depends upon the fact that formaldehyde combines with potassium cyanide in the sense of this equation:



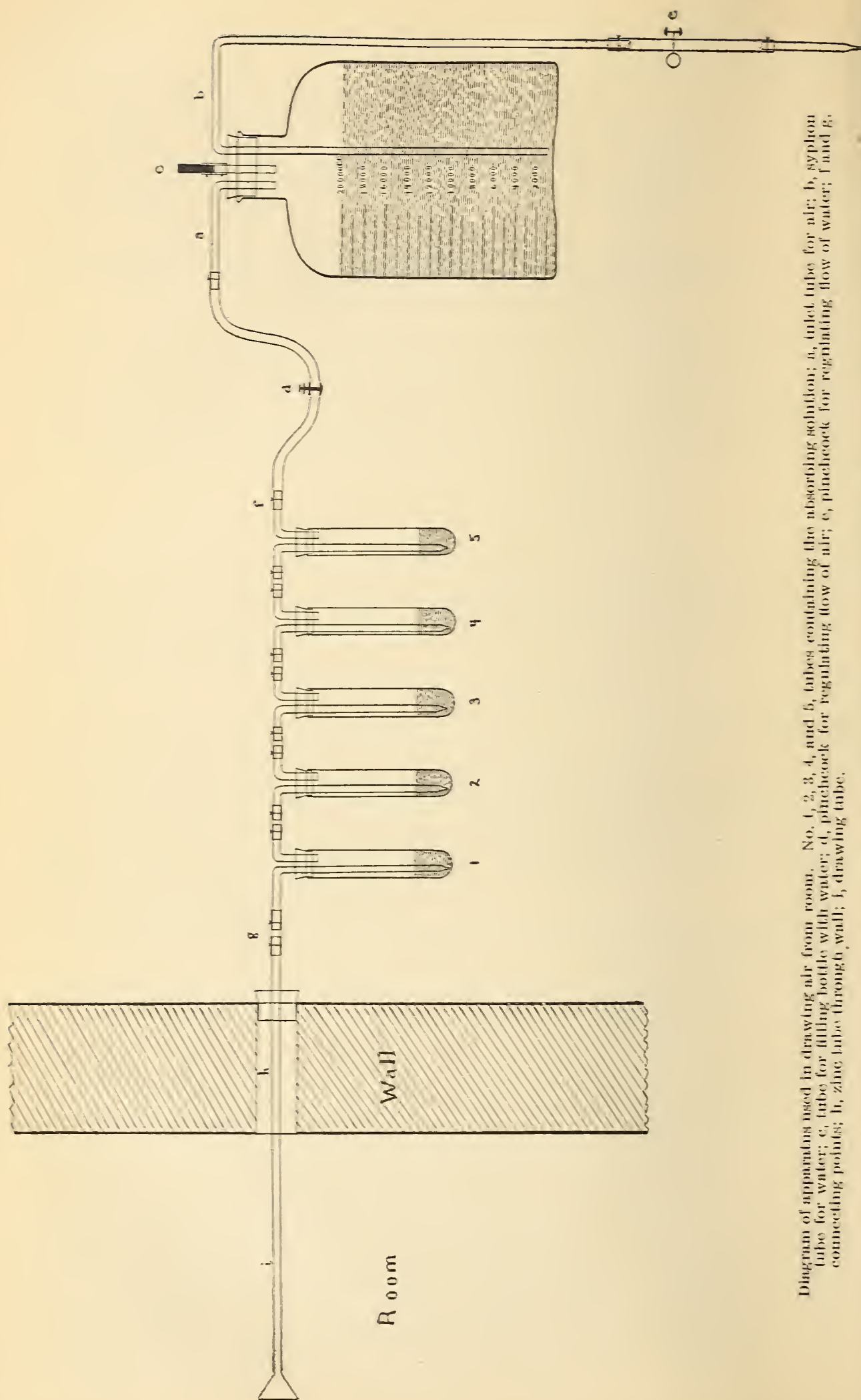
and that the cyanide thus combined can not be precipitated by means of silver nitrate. On the other hand the excess of potassium cyanide, over and above that required by the aldehyde, reacts with silver nitrate in the sense of this equation:



and hence can be determined quantitatively by means of decinormal solutions of silver nitrate and potassium sulphocyanate.

The potassium cyanide solution.—This is made by dissolving 3.3 gm. (of purity of 96 per cent or over) in water to the volume of 500 c. c. The solution is standardized against a decinormal solution of silver nitrate in the following manner:

Into a flask graduated to 100 c. c. an excess of the silver nitrate solution is drawn from a burette, say 12 or 13 c. c.; to this are added 4 or 5 drops of strong nitric acid (about 50 per cent), and then 10 c. c. of the cyanide solution from a burette. The flask is then shaken and filled up to the mark with water and the contents thoroughly mixed. The liquid is then filtered into a dry burette and 50 c. c. of the filtrate drawn into a beaker. To this is added some ferric ammonium alum indicator and the excess silver is titrated with a standard solution of potassium sulphocyanate in the usual way. The sulphocyanate solution must also be titrated against the silver solution in the presence of nitric acid and iron alum, to establish its equivalence to the silver nitrate. The number of c. c. of sulphocyanate required is multiplied by 2 and this is converted into its equivalent of decinormal silver nitrate solution. The latter is the excess of silver solution and the difference between it and the volume of silver solution originally taken



gives the number of c. c., to which 10 c. c. of potassium cyanide solution are equivalent.

In the titration of a dilute formaldehyde solution a definite volume or weight (known not to be in excess) is added to 10 c. c., or more if necessary, of the standard potassium cyanide solution. The latter, after stirring, is added to an acidified excess of decinormal silver nitrate solution, the whole made up to 100 c. c. or 200 c. c., and 50 or 100 c. c. of the clear filtrate titrated with sulphocyanate as above. From the amount of sulphocyanate required the volume of silver nitrate precipitated by potassium cyanide is calculated as above, and the difference between this and the volume of silver nitrate equivalent to the amount of cyanide solution originally taken is the number of c. c. of silver solution that represents the formaldehyde present; this number of c. c. multiplied by 0.003 (more exactly 0.002979) gives the weight of absolute formaldehyde, HCHO .

The silver cyanide precipitate must be removed before titrating an excess of silver by sulphocyanate, because it interferes with the sharpness of the end point and causes error.

In order now to determine the quantity of formaldehyde in the atmosphere of the room during any particular experiment a given volume of air, usually 10 liters, was drawn through a series of tubes containing a known amount of the standard solution of potassium cyanide or water by means of the apparatus shown in the cut facing this page. The quantity of formaldehyde absorbed under these conditions was determined in the manner already described. It was soon discovered that the air bubbling through the solution carried away a little hydrocyanic acid. To avoid loss of the latter the last tube containing the cyanide solution was followed by one containing silver nitrate solution, which effectually precipitated all the hydrocyanic acid carried over into it. The silver nitrate tube was followed by one containing distilled water. This tube showed no trace of hydrocyanic acid when tested by the ferric ferrocyanide reaction, and no formaldehyde when tested by Schiff's fuchsin-bisulphite reagent,^a or ammonia silver nitrate solution.

In preliminary experiments the contents of the silver nitrate tubes, after having passed formaldehyde-laden air through the series, were tested for formaldehyde to determine if any had escaped absorption in the cyanide tubes. To some of the liquid, about 2 c. c. of Schiff's reagent were added; a precipitate of silver chloride was produced, but no pink or purple color, indicating the absence of formaldehyde. For comparison the reagent was also added to a few c. c. of silver nitrate

^a Schiff's reagent: This is prepared by adding 20 c. c. of a solution of sodium bisulphite (sp. gr. 1.27) to 1,000 c. c. of aqueous fuchsin solution (1:1,000) and, after one hour, adding 10 c. c. of pure concentrated hydrochloric acid. It should be preserved in a well-stoppered bottle.

solution to which had been added a trace of formaldehyde; the contents of the tube soon acquired a pink color. It seemed evident that formaldehyde is wholly absorbed from air passing through a series of tubes containing cyanide solution. This conclusion was further strengthened by experiments on the absorption of formaldehyde from air by water alone, which will be mentioned presently.

It is a well-known fact that a solution of cyanide undergoes slow oxidation and other changes when exposed to the atmosphere, and it was suspected that in the experiments the long-continued bubbling of air through the solution would have the effect of diminishing its titre. It was found in several trials that when air was passed through 10 c. c. of a nearly decinormal solution of potassium cyanide at the same rate and for the same length of time as in the experiments its equivalent in decinormal silver nitrate was diminished by nearly 0.1 c. c. This correction was applied in the calculation of the result of each determination. Although it may not be absolutely correct, yet it can not be far from correct. As described above, the cyanide tube was followed by a tube containing silver nitrate, which latter was of course used in the subsequent titration.

After nearly all the results given further on had been obtained by the cyanide method, there came to our notice an article by Trillat,^a in which the author states that formaldehyde can be completely absorbed from air by passing it through a sufficient number of absorption apparatus containing water alone. This suggestion was put to the test, and it was found that three water tubes absorbed all of the formaldehyde, the last tube containing only a trace. The reason for not having chosen water at the start as an absorbing medium was that it was supposed a solution containing a substance, as cyanide, which could combine chemically with formaldehyde would be better suited as an absorbing agent than pure water. Owing to circumstances it was not possible to repeat all of the experiments and use water tubes to absorb the formaldehyde, but in several instances the absorption from the same charged air of the room was carried out in cyanide tubes and in water tubes, side by side. Although three tubes are sufficient, five tubes of water were used for greater precaution. In these parallel experiments the percentage results in the case of absorption by water were from 1.5 to 2 per cent higher than those in the case of absorption by cyanide.

We can not account for this difference, unless it is involved in the uncertainty of the correction made on account of the change of titre of the cyanide solution, due to air bubbling through it, which is referred to on page 12. Without making the correction, the two results were identical in some cases. It is possible also that the greater simplicity

^a Trillat, A.: Présence normal de la formaldéhyde dans les produits de la combustion incomplete. Rev. d'hyg., vol. 27, no. 2, Feb. 20, 1905.

in the case of the water tubes causes less error. At all events, although the results tabulated below may be 1.5 to 2 per cent less than the true ones, they are relatively correct. It would require too much space to give the calculation involved in obtaining each result tabulated below, but in order to give an idea of quantities of reagents used and method of carrying out the titrations one experiment will be described in full. It is one in which the air of the room was passed through cyanide solution and through plain water simultaneously.

(a) *Absorption in cyanide solution.*—

Tube 1 contained about 8 c. c. KCN solution.

Tube 2 contained about 5 c. c. KCN solution.

Tube 3 contained about 2 c. c. KCN solution.

Tube 4 contained about 8 c. c. $\frac{n}{10}$ AgNO₃.

Tube 5 contained about 10 c. c. distilled water.

Only the total quantity of cyanide need be measured, which, in this case, was exactly 15 c. c., distributed about as stated. There should not be less than 8 or 9 c. c. of cyanide solution in the first tube, lest there be an excess of uncombined formaldehyde in the liquid at the end of the absorption. Distilled water was added to the three cyanide tubes to make the column of liquid about 1.5 inches high, and to the silver nitrate tube to make a column about 1 inch high. The tubes were connected and air drawn through them as described above on page 12.

Volume of air drawn from room=10 liters.

Time required to draw air=1 hour, 4 minutes.

The five tubes were disconnected. Seven c. c. of $\frac{n}{10}$ AgNO₃ solution were introduced into a 250 c. c. flask and 8 or 10 drops of strong nitric acid (about 50 per cent). Through a funnel the silver-nitrate solution in tube 4 and its connecting tubes were carefully rinsed into the flask, followed in like manner by tubes 1, 2, and 3. Then the flask was filled to the mark with water and the contents thoroughly shaken. One hundred c. c. of the clear filtrate were titrated with sulphocyanate for excess of silver nitrate.

100 c. c. required 1.4 c. c. KCNS solution.

260 c. c. required 3.5 c. c. KCNS solution.

3.5 c. c. KCNS solution $\times 1.021 =$

3.57 c. c. $\frac{n}{10}$ AgNO₃ sol. = Excess present.

15.00 c. c. $\frac{n}{10}$ AgNO₃ sol. = Quantity taken.

Difference, 11.43 c. c. $\frac{n}{10}$ AgNO₃ sol. = Quantity combined with KCN.

15 c. c. KCNS solution $\times 0.954 =$

14.31 c. c. $\frac{n}{10}$ AgNO₃ sol. = Quantity that would have been required if formaldehyde

had not been absorbed.

11.43 c. c. $\frac{n}{10}$ AgNO₃ sol. = Quantity combined with KCN.

2.88 c. c. $\frac{n}{10}$ AgNO₃ sol. = the formaldehyde absorbed.

1c. c. $\frac{n}{10}$ AgNO₃ sol. represents 0.003 gm. formaldehyde.

Then, $0.003 \times 2.88 = 0.00864$ gm. formaldehyde in 10 liters of air. Therefore, 1 cu. ft. air (28.315 liters) contained 0.0245 gm. formaldehyde.

The titres of the sulphocyanate and cyanide solutions were as follows:

10 c. c. KCNS solution = 10.21 c. c. $\frac{n}{10}$ AgNO₃ solution.

10 c. c. KCN solution = 9.54 c. c. $\frac{n}{10}$ AgNO₃ solution.

(b) *Absorption in water.*—Tubes 1, 2, 3, 4, 5 contained a column of distilled water from 1 to 1.5 inches high. After making connections, air was drawn through them from the room, as already described.

Volume of air drawn from room = 10 liters.

Time required to draw air = 1 hr. 13 min.

Ten c. c. KCN solution were placed in a 300 c. c. beaker and the contents of the five tubes and their connections carefully rinsed into it. This solution was then transferred to a 250 c. c. flask containing 10.1 c. c. $\frac{n}{10}$ AgNO₃ solution plus 8 to 10 drops of nitric acid. The flask was filled to the mark with water and thoroughly shaken.

The subsequent procedure is exactly like that given under *a* above, except that not the corrected titre, but the original titre of the cyanide solution is used in the calculation, since the cyanide solution is not subjected to the action of air bubbling through it.

Volume of $\frac{n}{10}$ AgNO₃ solution corresponding to formaldehyde absorbed = 3.03 c. c. $3.03 \text{ c. c.} \times 0.003 = 0.00909$ gm. formaldehyde in 10 liters of air. One cu. ft. (28.315 liters) air contained 0.0257 gm. formaldehyde.

The quantity of formalin used to charge the room in nearly all the experiments, tabulated further on, was 600 c. c. of 35.66 per cent by volume—i. e., 100 c. c. of the formalin contained 35.66 gm. of absolute formalin. The strength was determined by the Blank and Finkenbeiner method of titration with hydrogen dioxide and caustic-soda solutions.^a In all the experiments the formalin was taken from the same supply.

In the two experiments just described 600 c. c. of formalin were used to charge the room. The results may be expressed in percentage,

^a For description see original article in *Berichte*, 1898, p. 2979, or the U. S. Pharmacopœia, Eighth Decennial Revision.

based on the amount of absolute formaldehyde taken per cubic foot of space in charging the room. The weight per cubic foot is

$$\frac{600 \text{ c. c.} \times 0.3566}{2000} = 0.107 \text{ gm. HCOH.}$$

In experiment *a* the per cent would be $\frac{0.0245 \times 100}{0.107} = 22.9$.

In *b* it would be $\frac{0.0257 \times 100}{0.107} = 24.01$.

If a correction were not applied in *a* the result would be the same as in *b*.

TEMPERATURE AND HUMIDITY.

In order to determine the temperature and humidity the sling psychrometer was used.^a This instrument consists of a pair of thermometers fastened to a piece of stiff sheet metal, provided with a handle at the end, by means of which the psychrometer can be rapidly whirled in the air. The bulb of one of the thermometers is covered with clean muslin, which before using is saturated with clean water. These two thermometers are known as the "dry" and "wet" bulb thermometer, respectively. After dampening the wet bulb the psychrometer is rapidly whirled in the air for a few seconds and then the reading of the two thermometers quickly taken. This is repeated until the readings are no longer changed by further whirling. The difference between the readings of the dry and wet bulb thermometers represents the depression of the wet-bulb thermometer, the degree of which is dependent upon the rate of evaporation, which in turn is dependent upon the amount of moisture in the atmosphere. The dry-bulb thermometer represents the temperature of the air.

Knowing the temperature of the air and the depression of the wet-bulb thermometer, the relative humidity and finally the absolute humidity of the air can be ascertained by reference to psychrometric tables for obtaining the vapor pressure, relative humidity, and temperature of the dew-point, prepared by the Weather Bureau, United States Department of Agriculture.^a

On account of the very important part that humidity plays in formaldehyde disinfection the method of calculating this factor in one case is here given, e. g.: After whirling the psychrometer the dry-bulb thermometer registers 80° F. and the wet-bulb thermometer 73° F. The temperature of the dry-bulb thermometer (80° F.) represents the temperature of the air, and 7° F. represents the difference between the dry and wet bulb thermometers. By referring to the tables for estimating the relative humidity, we find that this difference of 7° F. at a temperature of 80° F. represents a relative humidity of 72 per cent.

^aMarvin, C. F.: Psychrometric tables for obtaining the vapor pressure, relative humidity, and temperature of the dew-point. U. S. Weather Bureau, no. 235, Washington, 1900.

Going further, we find by reference to the tables for estimating the absolute humidity the weight of vapor in a cubic foot corresponding to a temperature of 80° F. and relative humidity of 72 per cent as follows:

	Grains.
At 80° F. and 70 per cent the weight is.....	7.654
The additional weight for 2 per cent is one-tenth the weight for 20 per cent, viz.....	.218
Hence the weight at 80° F. and 72 per cent is.....	7.872

As it was desired to know the temperature, relative and absolute humidity in our work in the room at certain stages of the experiment, and as the presence of the formaldehyde made it impossible to enter the room, the psychrometer was used in another way. After the handle was removed the psychrometer was fastened to a block of wood, which in turn was attached to the end of the shaft of a centrifuge passed through a small hole in one of the doors. By turning the crank of the centrifuge on the outside the psychrometer was rapidly revolved on the inside of the room. A cup of water was provided on the inside, so the wet bulb could be moistened, and a small window in the door just under the revolving apparatus made it possible to read the registration of the thermometers. By means of this apparatus the temperature, humidity, etc., of the room could be determined when desired. The results of whirling the psychrometer by this method were found on comparison to be practically the same as when used by hand.

BACTERIOLOGICAL METHODS.

The nonspore-bearing organisms, *Bacillus pyocyaneus*, *B. coli communis*, *B. typhosus*, *B. dysenterix* (Shiga), and *B. diphtherix*, were grown on agar slants at temperature of 37° C. for 24 hours before using.

For spores the *B. subtilis* was grown on agar slants about 40 days—a portion of the time at incubator temperature and the other portion at room temperature.

Different kinds of material were tried for exposing the organisms on—such as small pieces of blanket, linen, cotton, silk threads, filter paper, and glass—but it was found that filter paper and glass answered the purpose better than the others. and consequently were used throughout these experiments. It was found that in using a heavy material for this purpose sufficient formaldehyde would at times be carried over into the tube of nutrient bouillon in which they were planted to inhibit bacterial growth. This was especially so if the pieces of material used were of considerable size.

The slips of filter paper and pieces of glass used were about 0.5 cm. square and were sterilized before contaminating with the organism. An emulsion of the organism to be used was made in sterilized water

and the slips of filter paper and pieces of glass placed in Petri dishes and saturated with the emulsion. The dishes were then placed in the incubator room at a temperature of 37° C. for one hour, the slips of filter paper and pieces of glass being small, and as they were moved about in the Petri dishes from time to time during the hour this seemed ample time to thoroughly dry them.

The other method used for making the exposures in these experiments is one first used by Doctor Wilson,^a and which will be called in this work the "Wilson method." As used in these experiments it consisted of a heavy piece of cardboard about 4 by 15 cm. folded in the middle like the cover of a small book and having a small piece of filter paper about 0.5 by 4 cm. pasted by one end inside of it something like the leaf of a book. This left the other end of the filter paper unattached. This end was contaminated with the organism to be exposed.

A small nick in the filter paper about 0.5 cm. from this end facilitated tearing off the end with forceps when so desired. A number of these little devices were prepared in this way and sterilized in a hot-air sterilizer. The free ends of the filter paper were moistened with a watery suspension of the organism and dried in the incubator room for one hour as with the other methods above described.

The organisms were then ready to be exposed to the action of the formaldehyde gas.

The exposures were made in the wire trays in the room which have been described.

The trays, being immovable, were easily sterilized in a gas flame. The slips of filter paper and pieces of glass were carefully placed in the trays by means of sterile forceps, care being taken not to have any two pieces in contact with each other.

The exposures with the Wilson method were also made on these trays.

As no appreciable difference in the germicidal action of the formaldehyde on exposures made at different heights in the room was observed, most of the exposures, for convenience, were made through the middle series of zinc tubes.

After the organism had been exposed to the action of the formaldehyde the desired time, the rubber stopper was removed and the wooden frame carrying the wire tray momentarily withdrawn far enough to procure one of the exposures.

The slips of filter paper and pieces of glass were removed with sterile forceps and planted in tubes of nutrient bouillon. With the Wilson method the slips of filter paper were torn off with sterile forceps and planted in the same way.

^aRobert J. Wilson, M. D., assistant director of the Research Laboratory, New York City Department of Health.

In this manner plants into tubes of nutrient bouillon were made at different intervals when so desired. The tubes were placed in the incubating room at a temperature of 37° C. and the results recorded after ten days' incubation.

Other methods of exposing organisms, such as placing slips of contaminated filter paper in envelopes and in small paper boxes in which numerous holes had been punched, were tried for the purpose of testing the penetrating power of formaldehyde, but the results were so unsatisfactory that the methods were abandoned.

The Wilson method affords a very simple and convenient way of exposing organisms to the action of a gaseous disinfectant, and in case it is impracticable to make the plants immediately after making the exposures they can be taken to the laboratory and planted without much risk of outside contamination.

**DISINFECTANTS AUTHORIZED BY U. S. QUARANTINE REGULATIONS AND THE PROPER
METHODS OF GENERATING AND USING SAME.**

FORMALDEHYDE GAS.

163. Formaldehyde gas is effective if applied by one of the methods given below. Formaldehyde gas has the advantage as a disinfectant that it does not injure fabrics or most colors. It is not poisonous to the higher forms of animal life. It fails to kill vermin such as rats, mice, roaches, bedbugs, etc. The method is not applicable to the holds of large vessels. Formaldehyde is applicable to the disinfection of rooms, clothing, and fabrics, but should not be depended upon for bedding, upholstered furniture, and the like, when deep penetration is required.^a

164. Many formaldehyde solutions do not contain 40 per cent of formaldehyde, and all are apt to deteriorate with time. It is therefore necessary to use a quantity in excess of the amount prescribed in these regulations, unless the solution has been recently analyzed.

165. The following methods of evolving the gas may be used:

- (a) Autoclave under pressure, 3 to 12 hours' exposure.
- (b) Lamp or generator, 6 to 18 hours' exposure.
- (c) Spraying, 12 to 24 hours' exposure.
- (d) Formaldehyde and dry heat in partial vacuum, 1 hour's exposure.

166. The minimum number of hours' exposure as given above applies to empty rooms of tight construction containing smooth, hard surfaces; the maximum number of hours' exposure applying in all cases to textiles and other articles of a similar kind requiring more or less penetration.

167. Autoclave under pressure. This method has considerable penetrating power when applied as detailed below. Rooms or apartments

^a It should be noted that formaldehyde disinfection is more efficient in warm, moist, or still weather than in cold, dry, or windy weather.

need no special preparation beyond the ordinary closing of doors and windows. Pasting, caulking, or chinking of ordinary cracks and crevices is not necessary. The doors of lockers and closets and the drawers of bureaus should be opened. In this apparatus use formalin (40 per cent), with the addition of a neutral salt, such as calcium chloride (20 per cent). The gas must be evolved under a pressure not less than 45 pounds. After the gas is separated from its watery solution the pressure may be allowed to fall and steam projected into the compartment to supply the necessary moisture. Use not less than 10 ounces of formalin per 1,000 cubic feet, and keep the room closed for three to twelve hours after the completion of the process. For large rooms the gas must be introduced at several points as far apart as possible. It is applicable to the disinfection of clothing and fabrics suspended loosely in such a manner that every article is freely accessible to the gas from all directions.

168. Lamp or generator. This method requires an apparatus producing formaldehyde by a partial oxidation of wood alcohol, and in using it the room or apartment should be rendered tight as practicable. Oxidize 24 ounces of wood alcohol per 1,000 cubic feet, and keep the room closed for six to eighteen hours, in accordance with the provisions of paragraph 165. This method leaves little or no odor. When applied to clothing and textiles, the articles should be suspended in a tight room and so disposed as to permit free access of the gas. (See also Par. 166.) The wood alcohol should be of 95 per cent strength, and should not contain more than 5 per cent of acetone.

169. Spraying. The formalin (40 per cent) should be sprayed on sheets suspended in the room in such a manner that the solution remains in small drops on the sheet. Spray not less than 10 ounces of formalin (40 per cent) for each 1,000 cubic feet. Used in this way a sheet will hold about 5 ounces without dripping or the drops running together. The room must be very tightly sealed in disinfecting with this process, and kept close not less than twelve hours. The method is limited to rooms or apartments not exceeding 2,000 cubic feet. The formalin may also be sprayed upon the walls, floors, and objects in the rooms.

170. Formaldehyde with dry heat in partial vacuum. This method has superior penetrating powers and is specially applicable to clothing and baggage. The requirements of this method are (1) dry heat of 60° C. sustained for one hour; (2) a vacuum of 15 inches; (3) formaldehyde evolved from a mixture of formalin with a neutral salt, in an autoclave under pressure, using not less than 30 ounces of formalin (40 per cent) for 1,000 cubic feet; and (4) a total exposure, under these combined conditions, of one hour.

171. The stated times of exposure to sulphur dioxide and formaldehyde are sufficient to destroy bacterial infection due to non-spore-

bearing organisms, providing that the infection is present on the surface. If the room is of peculiar construction, so as to impede the diffusion of the gas, or if the room is a dirty one, or if on account of any other condition rendering the germicidal action of the gas more difficult, the time of exposure should be proportionately increased, or supplanted by other methods.

DIFFERENT METHODS OF EVOLVING FORMALDEHYDE GAS.^a

I. FORMALIN-PERMANGANATE METHOD.

When formalin is poured upon crystals of potassium permanganate, a vigorous reaction takes place, accompanied by strong ebullition of the liquid and sufficient heat to produce a large quantity of formaldehyde gas, water vapor, etc. The time required for the reaction to begin, or at least to become apparent, varies from a few seconds to a minute or two, depending upon the temperature.

The reaction is apparently over in a comparatively short time (about five minutes), and with proper proportion of substances the residue in the vessel is almost dry. Evans and Russell used the proportion of 100 c. c. of formalin to 37.5 grams of permanganate, but we found that with this proportion considerable formalin remained in the residue, as was evidenced by its wet condition and powerful odor of formaldehyde. After some experimenting we adopted the proportion of 100 c. c. of formalin to 50 grams of permanganate, which gave a residue fairly free from liquid.

The quantity used to charge the room of 2,000 cubic feet was in nearly all cases 600 c. c. of formalin (containing 35.66 per cent of formaldehyde by volume). The generator was a galvanized-iron pail 10 inches in diameter and 10 inches deep, holding 12 liters (3 gallons). The pail was placed in the center of the room, the permanganate dropped into it and the formalin quickly poured upon it. The ebullition was so vigorous that the frothy mass often reached nearly to the top of the pail.

We did not investigate the exact nature of the chemical reaction that took place, as for our purposes we were only interested in the fact that an abundance of formaldehyde was given off in gaseous form. According to Evans and Russell, "analysis of the gas thrown out into a room by this reaction showed it to consist of formaldehyde, water vapor, carbon dioxide, and a very small amount of formic acid. In the generator were found a lower oxide of manganese, a little formaldehyde, carbon dioxide, potassium hydroxide, and, I think, a little potassium formate resulting from the neutralization

^a In the experiments which follow, the quantities of formalin employed for the evolution of formaldehyde gas have been in strict accordance with the U. S. Quarantine regulations. In the case of the formaldehyde generating lamp, the quantities of methyl alcohol used have been less than those prescribed by the regulations; about 10 per cent less in the experiments in Pullman cars and about 30 per cent less in the room experiments.

of the potassium hydrate by formic acid." It seems highly probable that the decomposition takes place essentially according to the following reaction: $4\text{KMnO}_4 + 3\text{HCHO} + \text{H}_2\text{O} = 4\text{MnO}(\text{OH})_2 + 2\text{K}_2\text{CO}_3 + \text{CO}_2$ (CO_2), and that the heat resulting from this reaction causes the liberation of formaldehyde gas from the remaining portion of the formalin.

The reaction is more rapid the more finely powdered the permanganate crystals are, but in our experiments we used the small needle crystals of commerce without further powdering.

The temperature and relative humidity of the air in the room were recorded before as well as at definite intervals after mixing the formalin and permanganate. This showed a considerable amount of moisture given off by the process.

Many variations and conditions might have been tried, such as covering the pail with sheet asbestos to retain the heat, heating the pail before the experiment or placing it in hot water, powdering the permanganate crystals, etc., but as time is a factor we adopted those conditions which are least difficult to execute in disinfecting rooms.

Before a new charge was put into the room all formaldehyde of the previous experiment was got rid of by opening the doors and windows until no odor of formaldehyde was perceptible.

Chemical determinations.—In making these determinations approximately fifteen minutes were allowed to elapse after mixing the formalin and permanganate before beginning to draw air from the room. This seemed ample time for the reaction to cease and for the formaldehyde gas to diffuse through the air of the room. The results are shown in the following table:

TABLE 1.—*Experiments with the formalin-permanganate method.*

Number.	Temperature of room before experiment.	Formalin (35.66 per cent by volume).	KMnO_4 .	Time between mixing and drawing air.	Time required to draw air.	Volume of air drawn, in liters.	Relative humidity before experiment.	Relative humidity 10 minutes after mixing.	Increase in grains of moisture per cubic foot.	Abs. formaldehyde used per cubic foot.	Abs. formaldehyde found per cubic foot.	Per cent yield.	Condition of wind, etc.
	° F.	c. c.	gm.	h. m.	h. m.					gm.	gm.		
I	71	600	300	a 14	1 10	10	72	86	1.47	0.107	0.04035	37.70	Moderate wind.
				b 3 38	1 21	10107	.0243	22.7	Do.
II	69	800	400	a 12	1 32	10	63	86	2.0	.1426	.0505	35.41	Slight breeze.
				b 22 17	1 10	111426	.01722	12.07	Very slight breeze.
III	77	400	200	15	1 12	10	79	85	0.58	.0713	.025	35.06	Moderate wind.
IV	79	600	300	17	1 21	10	79	94	1.72	.107	.0419	39.15	Practically no wind; windows and doors of room pasted up.
V	62	600	300	15	1 15	10	55	74	1.17	.107	.02685	25.1	No breeze.
VI	52	600	300	15	1 20	10	63	78	.54	.107	.01186	11.09	No wind.

Although the room in which the experiments were made was zinc-lined and the doors and windows were fairly close fitting, still it was not air-tight, so that the conditions were not of that exact quantitative character as obtains in an operation like the precipitation of sulphuric acid by barium chloride. In view of this condition of the room, which, of course, allowed the winds to exert a varying influence upon the rate of leakage therefrom, the percentages obtained in those experiments performed under approximately the same conditions as to temperature can be considered as agreeing fairly well. The results also indicate that the relation between the formalin and permanganate in the ratio taken is fairly quantitative and that the percentage yield of formaldehyde gas is approximately the same whether 400, 600, or 800 c. c. be taken for a charge. Experiments Ib and IIb table give an idea of the rate of leakage of formaldehyde from the room. In III, where the room was made more air-tight by pasting paper over the cracks of the door and covering the window frames, the per cent is a little higher.

The percentage yield of formaldehyde with this method is very much affected by certain variations in the temperature. This, however, is not the case with experiments done at temperatures above 60° to 65° F. The results then agree rather closely, and it is probable that with this condition of temperature on a very quiet day with a charge of 600 c. c. formalin (35.66 per cent by volume) the weight of the gas in the room would be between 38 and 39 per cent of the weight in the 600 c. c. of formalin used. This percentage is only slightly less than that obtained under similar conditions with the retort and autoclave methods.

Effects of low temperature upon the state of the formaldehyde in the room.—Provided the temperature is below 60° or 65° F., the liberation of formaldehyde by this method produces a hazy or foggy condition of the air in the room. This is most marked just after the process of liberation is complete; but it does not entirely disappear during the time required to do an experiment, usually three hours. The lower the temperature in the room the more marked is this condition, which apparently is due to some change in the formaldehyde, resulting from the effects of cold upon it and to a certain extent to the presence of the aqueous vapor liberated. The latter, however, would soon become invisible.

The exact change that takes place in the formaldehyde is not plain, but evidently there is much polymerization, as is shown by the paraform deposited in the room after the experiment is completed.

The hazy condition in the room is about the same with the formalin-permanganate method as with the retort and autoclave; but the deposit of paraform is more noticeable with the former than the latter two methods.

This change of state in the formaldehyde, of course, very materially reduces the percentage obtained in our determinations, as is shown in experiments VI and VII, table 1. In VI, as the temperature (62° F.) was close to the point where polymerization seems to begin, 25.1 per cent was found; but in VII (temperature 52° F.) only 11.09 per cent was obtained.

These results can not be interpreted as positively representing the percentage of gas actually existing as such in the air during the time the determinations were made, since it is possible that all the paraform or other changed formaldehyde was not eliminated from the determinations, although a small pledget of cotton was placed in the funnel of the drawing tube to prevent the paraform, etc., from passing out in the air drawn. The cotton pledget was placed in the funnel of the drawing tube only when working at a reduced temperature and when some polymerization was apparent.

Germicidal properties.—For the purpose of determining the germicidal properties of formaldehyde liberated by this method the organisms were placed in the wire trays in the room before mixing the formalin and permanganate, and the time of exposure counted from the time the reaction and liberation of the formaldehyde began.

As most of the gas is given off in the first minute or two, the reason for this is evident.

The method of preparing the organisms, making the exposures, etc., have been described. A summary of conditions and results is given in each of the following experiments:

EXPERIMENT NO. 1.

Formalin-permanganate method.

Formalin, 400 c. c.

Permanganate, 200 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.0713 gram.

Quantity of formaldehyde found per cubic foot, 0.025 gram.

(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate, and consuming 1 hour 12 minutes in the drawing.)

Yield of formaldehyde, 35.06 per cent.

Weather: Moderate breeze from west; almost clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	77	79	7.88
After 10 minutes.....	77	85	8.46
After 2 hours.....	78	79	8.12

NOTE.—In all the experiments with this method the temperature, humidity, and time of exposure of organisms are given from the moment of mixing the formalin and permanganate.

EXPERIMENT NO. 1—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	15	30	45	60	120
<i>B. pyocyaneus</i>	Filter paper.....	—	—	—	—	—	—
<i>B. coli communis</i>do.....	—	—	—	—	—	—
<i>B. dysenteriae</i>do.....	+	—	—	—	—	—
<i>B. subtilis</i>do.....	+	+	—	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	—	—
<i>B. subtilis</i>do.....	+	+	+	+	+	—

EXPERIMENT NO. 2.

Formalin-permanganate method.

Formalin, 600 c. c.
Permanganate, 300 grams.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Quantity of formaldehyde found per cubic foot, 0.0419 gram.
(Determination made by drawing air from the room, beginning 17 minutes after mixing the formalin and permanganate, and consuming 1 hour 21 minutes in the drawing.)
Yield of formaldehyde, 39.15 per cent.
Weather: Practically no wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	79	79	8.39
After 10 minutes.....	79.5	94	10.10
After 1 hour.....	79.5	89	9.57

See Note, Experiment No. 1.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	15	20	30	45	60
<i>B. pyocyaneus</i>	Filter paper.....	—	—	—	—	—	—	—
<i>B. coli communis</i>do.....	—	—	—	—	—	—	—
<i>B. dysenteriae</i>do.....	+	—	—	—	—	—	—
<i>B. subtilis</i>do.....	+	+	+	+	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—	—
<i>B. subtilis</i>do.....	+	+	+	+	+	+	—

EXPERIMENT NO. 3.

Formalin-permanganate method.

Formalin, 600 c. c.

Permanganate, 300 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.0353 gram.

(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate and consuming 1 hour 15 minutes in the drawing.)

Yield of formaldehyde, 33 per cent.

Weather: Strong wind from the southwest; clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	77.5	72	7.28
After 10 minutes.....	78.0	87	8.94
After 1 hour.....	78.0	81	8.30

See Note, Experiment No. 1.

[+ means growth; - no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	15	20	30	45	60
<i>B. pyocyaneus</i>	Filter paper.....	+	+	-	-	-	-	-
<i>B. coli communis</i>	do.....	+	-	-	-	-	-	-
<i>B. dysenterix</i>	do.....	+	+	-	-	-	-	-
<i>B. subtilis</i>	do.....	+	+	+	-	-	-	-
<i>B. coli communis</i>	Wilson method.....	+	+	-	-	-	-	-
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	-

EXPERIMENT NO. 4.

Formalin permanganate method.

Formalin, 600 c. c.

Permanganate, 300 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde liberated, undetermined.

Weather: Cloudy; light westerly winds.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	78	75	7.70
After 10 minutes.....	78	91	9.34
After 2 hours.....	78	91	9.34

See Note, Experiment No. 1.

EXPERIMENT NO. 4—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.				
		5	10	20	30	60
<i>B. coli communis</i>	Glass	—	—	—	—	—
<i>B. subtilis</i>	do	—	—	—	—	—
<i>B. pyocyaneus</i>	Filter paper	—	—	—	—	—
<i>B. typhosus</i>	do	+	—	—	—	—
<i>B. coli communis</i>	do	+	—	—	—	—
<i>B. subtilis</i>	do	—	—	—	—	—
<i>B. coli communis</i>	Wilson method	+	—	—	—	—

The minimum temperature and relative humidity in the foregoing experiments were 77° F. and 72 per cent, respectively; under these conditions the germicidal results were very satisfactory. The non-spore-bearing organisms exposed on slips of filtered paper and pieces of glass were killed within a few minutes. The spores of *B. subtilis* exposed in the same manner were likewise killed within a comparatively short time. The time required to kill the same organisms exposed by the Wilson was more than twice as long as that required with the other methods of exposure.

Although only 400 c. c. of formalin were used in Experiment No. 1, the results are about the same as with the other experiments in which 600 c. c. were used. Comparing this same experiment (No. 1) with the following one (No. 5) in which 800 c. c. of formalin were used, the germicidal results of exposures on filter paper are in favor of the former experiment, due to the higher temperature and humidity in this experiment; the results of exposures by the Wilson method are in favor of the latter experiment, due in all probability to the increased percentage of formaldehyde in the air, favoring penetration.

EXPERIMENT NO. 5.

Formalin-permanganate method.

Formalin, 800 c. c.

Permanganate, 400 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.1426 gram.

Quantity of formaldehyde found per cubic foot, 0.0505 gram.

(Determination made by drawing air from the room, beginning 12 minutes after mixing the formalin and permanganate, and consuming 1 hour 32 minutes in the drawing.)

Yield of formaldehyde, 34.41 per cent.

Weather: Light, westerly wind; almost clear.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	69	63	4.86
After 10 minutes	70	86	6.86
After 1 hour	70	81	6.46

See Note, Experiment No. 1.

EXPERIMENT NO. 5—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	10	20	30	40	60
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—	—
<i>B. typhosus</i>	do.....	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	+	—	—	—
<i>B. dysenteriae</i>	do.....	+	+	—	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—	—

EXPERIMENT NO. 6.

Formalin-permanganate method.

Formalin, 600 c. c.

Permanganate, 300 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.04035 gram.

(Determination made by drawing air from the room, beginning 14 minutes after mixing the formalin and permanganate, and consuming 1 hour 10 minutes in the drawing.)

Yield of formaldehyde, 37.70 per cent.

Weather: Moderate northwest wind, clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	71	45	3.70
After 10 minutes.....	72	60	5.10
After 20 minutes.....	72	58	4.93
After 2 hours.....	72	55	4.68

See Note, Experiment No. 1.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	20	45	60	90	120
<i>B. coli communis</i>	Glass.....	+	+	+	—	—	—	—
<i>B. pyocyaneus</i>	Filter paper.....	+	+	+	+	—	—	—
<i>B. typhosus</i>	do.....	+	+	+	+	—	—	—
<i>B. coli communis</i>	do.....	+	+	+	+	+	—	—
<i>B. dysenteriae</i>	do.....	+	+	+	+	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+

The preceding experiment (No. 6) shows the effects of a relatively low humidity upon the germicidal power of the formaldehyde. Although the temperature in this experiment was comparatively high the time required to kill was much prolonged as compared with the experiments in which the temperature and humidity were both high.

The time to kill is comparatively longer with the Wilson method of making exposures than with the other methods; this fact may be attributed to the lower humidity diminishing the power of penetration of the formaldehyde.

The following two experiments show the inefficient results obtained when the temperature is comparatively low. No doubt slightly better results would have been obtained in these two experiments if the humidity had been higher, say 90 per cent. In Experiment No. 7, temperature 62° F., some polymerization of the formaldehyde took place, as was evidenced by the hazy appearance of the air in the room and the decreased percentage of formaldehyde obtained; but it was not nearly so marked as in Experiment No. 8, temperature 52° F. In the latter experiment quite a deposit of paraform was observed in the room after opening.

EXPERIMENT NO. 7.

Formalin-permanganate method.

Formalin, 600 c. c.
Permanganate, 300 grams.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Quantity of formaldehyde found per cubic foot, 0.02685 gram.
(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate and consuming 1 hour 15 minutes in the drawing.)
Yield of formaldehyde, 25.1 per cent.
Weather: Cloudy, no wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	62	55	3.37
After 10 minutes.....	62	74	4.54
After 3 hours.....	62	64	3.93

See note, Experiment No. 1.

[+ means growth; - no growth.]

Organism.	How exposed	Time of exposure in minutes, and results.							
		10	20	30	45	60	90	120	180
<i>B. coli communis</i>	Filter paper.....	+	-	-	-	-	-	-	-
<i>B. typhosus</i>	do.....	-	-	-	-	-	-	-	-
<i>B. subtilis</i>	do.....	+	+	+	+	-	-	-	-
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+	-	-
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+	+

EXPERIMENT NO. 8.

Formalin-permanganate method

Formalin, 600 c. c.

Permanganate, 300 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.01186 gram.

(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate and consuming 1 hour 20 minutes in the drawing.)

Yield of formaldehyde, 11.09 per cent.

Weather: Rainy, very little wind.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	52	63	2.75
After 10 minutes	51	78	3.29
After 3 hours	50	71	2.89

See note, Experiment No. 1.

[+ means growth; - no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.							
		10	20	30	45	60	90	120	180
<i>B. coli communis</i>	Filter paper	+	+	+	-	-	-	-	-
<i>B. typhosus</i>	do	+	+	-	-	-	-	-	-
<i>B. subtilis</i>	do	+	+	+	+	+	+	+	-
<i>B. coli communis</i>	Wilson method	+	+	+	+	+	+	+	+
<i>B. subtilis</i>	do	+	+	+	+	+	+	+	+

The results with the formalin-permanganate method are all that can be desired for practical disinfection purposes, provided the temperature and relative humidity are comparatively high. Under these conditions no particular advantage is gained, especially for surface disinfection, by having a large quantity of formaldehyde gas present, as is shown by the above experiments in which different quantities of formalin were used. With a low temperature or humidity formaldehyde is practically useless as a disinfectant.

The minimum percentage of humidity and lowest temperature at which disinfection with formaldehyde can be accomplished can not be stated accurately, as the one depends to a limited extent upon the other. However, it seems that for practical disinfection with the formalin-permanganate method the humidity should not be below 60 or 65 per cent and the temperature not below about 65° F. The former refers to the percentage of humidity in the air of the room before starting an experiment. In our experiments the humidity in the air of the room was increased 15 to 23 per cent in the different experiments by the moisture given off from the formalin-permanganate. Just what part this increase in humidity plays in disinfecting

with formaldehyde can not be stated exactly; but the indications are that too much dependence must not be placed in it. No doubt it is an advantage, but it does not seem to answer the purpose so well as the natural humidity of the atmosphere.

The special points of advantage of the formalin-permanganate method of evolving formaldehyde are that it is simple in operation, no special apparatus is required, it is economical both as to time and money, it produces considerable moisture, and it liberates a large quantity of formaldehyde in a relatively short time. This last fact is of special advantage, since with an ordinary room no pasting of cracks, etc., is required. For disinfection purposes it is better to have a large quantity of formaldehyde with a short exposure than a small quantity with a long exposure. A large quantity of formaldehyde and a high temperature and humidity all assist penetration.

II. DILUTED FORMALIN AND PERMANGANATE METHOD.

A number of experiments were made with formalin diluted with various quantities of water and different weights of permanganate.

The purpose in adding the water was to increase, if possible, the amount of moisture given off.

In each experiment 600 c. c. of formalin were used, to which were added, before mixing with the permanganate, 300 c. c. of water in some of the experiments and 600 c. c. in the others.

For every 100 c. c. of water used an additional 25 grams of permanganate were required in order to obtain a residue fairly free from liquid.

The time required for the reaction to begin was slightly diminished in this method as compared with the undiluted formalin-permanganate method. The ebullition, too, seemed to be more violent.

Except for the differences above noted, the method of procedure in charging the room was the same as with the undiluted formalin-permanganate method already described.

Chemical determinations.—The interval between setting off the charge and beginning to draw air, the volume of air drawn (10 liters) and the time required to draw it were about the same as in Table 1. In several instances two experiments were made simultaneously with 5 and 10 liters of air respectively.

The results are shown in the following table:

TABLE 2.—*Experiments with the diluted formalin-permanganate method.*

Number.	Temperature of room before experiment.	Formalin (35.66 per cent by volume).	Water.	KMnO ₄ .	Time between mixing and drawing air.	Time required to draw air.	Volume of air drawn, in liters.	Relative humidity before experiment.	Relative humidity 10 minutes after mixing.	Increase in grams of moisture per cubic foot.	Abs. formaldehyde used per cubic foot.	Abs. formaldehyde found per cubic foot.	Per cent yield.	Condition of wind, etc.
	°F.	c. c.	c. c.	gm.	h. m.	h. m.					g. m.	g. m.		
I	81	600	600	450	17 0	a 1 20 b 1 20	10 10	81	94	1.79107 .107	.0272 .0272	25.4 25.4	Slight breeze. Do.
II	81	600	300	450	16 0	1 5	10	83	98	2.06	.107	.03081	28.8	Moderate wind.
III	81.5	600	300	300	16 0	a 1 9 b 1 8	5 10	74	94	2.28107 .107	.0242 .02336	22.6 21.8	Do. Do.
IV	81	600	300	375	14 0	a 0 45 b 1 14	5 10	77	96	2.14107 .107	.0289 .02965	27 27.7	Brisk wind. Do.
V	85	600	300	375	15 0	a 0 34 b 1 5	5 10	70	90	2.55107 .107	.03755 .0356	35.1 33.27	Gentle breeze. Do.
VI	85	600	300	375	a 0 17 b 0 17 c 2 27 d 4 24 e 24 33	0 42 1 20 1 18 1 0 1 23	5 10 10 10 10	70	88	2.3107 .107 .107 .107 .107	.0341 .03296 .02548 .02276 .01028	31.84 30.80 23.81 21.27 9.6	Do. Do. Do. Do. Do.
VII	79	600	300	375	a 0 21 b 0 21 c 4 7 d 23 46	0 47 1 17 1 18 1 13	5 10 10 10	79	94	1.72107 .107 .107 .107	.03517 .03517 .02658 .01546	32.87 32.87 24.84 14.44	Practically no wind; windows and doors pasted up with paper.
VIII	39	600	300	375	0 15	1 5	10	51	92	.54	.107	.01626	15.2	
IX	41	600	600	450	0 15	1 30	11	55	92	.89	.107	.01334	11.53	

Of the various proportions used that of 600 c. c. formalin, 300 c. c. water, and 375 gms. of permanganate gives the highest yield of formaldehyde gas.

In experiment I the determinations *a* and *b*, made simultaneously in the same time and on the same volume of air, gave the same results; this would seem to indicate that the method of analysis, under the same conditions, gives constant results. In experiment III 5 liters of air in *a* were drawn in the same time as 10 liters in *b*, with practically the same result; this seems to point to the conclusion that 5 liters of air is a large enough quantity for a determination.

In experiments IV, V, VI, and VII, the same proportions of materials were used to charge the room, but the results in IV are low on account of the brisk wind blowing at the time and should not be compared with those of V, VI, and VII. The three determinations of V, VI, and VII, which are comparable, show a fairly close agreement. VI and VII show the rate of leakage from the room, and *d* and *e* of VI and *c* and *d* of VII, which are comparable, show that when there is a very little wind the leakage from the room when pasted up with paper is not much less than when not so pasted.

A reduction in temperature produces about the same hazy appearance in the room that is observed in case of the undiluted formalin-permanganate, retort, and autoclave methods, but the deposit of paraform is less than in the undiluted formalin-permanganate method. This result may be due to the decreased percentage of formaldehyde which is given off or to the decreased polymerization attendant upon the amount of water added. The percentages obtained by the diluted formalin-permanganate method are relatively higher, considering the temperatures, than is the case with the undiluted formalin-permanganate method, as will be seen by comparing experiments VIII and IX, Table 2, with VI and VII, Table 1. The difference in percentage obtained in experiments VIII, temperature 39° F. (15.2 per cent) and IX, temperature 41° F. (11.53 per cent), Table 2, is probably due to the larger quantity of water added in the latter experiment.

Germicidal properties.—The method of procedure was the same as with the undiluted formalin-permanganate method already described. A summary of conditions and results is given in each of the following experiments:

EXPERIMENT NO. 9.

Dilute formalin-permanganate method.

Formalin, 600 c. c.
Water, 600 c. c.
Permanganate, 450 grams.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Quantity of formaldehyde found per cubic foot, 0.0272 gram.
(Determination made by drawing air from the room, beginning 17 minutes after mixing the formalin and permanganate, and consuming 1 hour 20 minutes in the drawing.)
Yield of formaldehyde, 25.4 per cent.
Weather: Light northerly breeze, clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	81	81	9.13
After 10 minutes.....	82	94	10.92
After 2 hours.....	82.5	90	10.62

NOTE.—In all the experiments with this method the temperature, humidity, and time of exposure of organisms are given from the moment of mixing the formalin and permanganate.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in min- utes, and results.					
		5	10	25	45	60	120
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—	—
<i>B. dysenterix</i>	do.....	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—

EXPERIMENT NO. 10.

Dilute formalin-permanganate method.

Formalin, 600 c. c.

Water, 600 c. c.

Permanganate, 450 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.0279 gram.

(Determination made by drawing air from the room, beginning 16 minutes after mixing the formalin and permanganate, and consuming 1 hour 12 minutes in the drawing.)

Yield of formaldehyde, 26.1 per cent.

Weather: Light east wind, cloudy.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	80	74	8.09
After 10 minutes.....	81	91	10.82
After 2 hours.....	81	91	10.26

See note, Experiment No. 9.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	10	20	30	60	120
<i>B. coli communis</i>	Glass.....	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	—	—	—	—	—	—
<i>B. pyocyaneus</i>	Filter paper.....	—	—	—	—	—	—
<i>B. dysenteriae</i>	do.....	+	—	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—	—
<i>B. subtilis</i>	do.....	—	—	—	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—

EXPERIMENT NO. 11.

Dilute formalin-permanganate method.

Formalin, 600 c. c.

Water, 300 c. c.

Permanganate, 375 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.03517 gram.

(Determination made by drawing air from the room, beginning 21 minutes after mixing the formalin and permanganate, and consuming 47 minutes in the drawing.)

Yield of formaldehyde, 32.87 per cent.

Weather: Light breeze, cloudy.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	79	79	8.38
After 10 minutes.....	79.5	94	10.10
After 2 hours.....	80	89	9.57

See note, Experiment No. 9.

EXPERIMENT NO. 11—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.				
		5	10	20	30	60
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—
<i>B. dysenteriae</i>	do.....	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—

EXPERIMENT NO. 12.

Dilute formalin-permanganate method.

Formalin, 600 c. c.

Water, 300 c. c.

Permanganate, 375 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.0289 gram.

(Determination made by drawing air from the room, beginning 14 minutes after mixing the formalin and permanganate, and consuming 45 minutes in the drawing.)

Yield of formaldehyde, 27 per cent.

Weather: Moderate east wind, rainy.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	81	77	8.26
After 10 minutes.....	81	96	10.82
After 2 hours.....	82	88	10.23

See note, Experiment No. 9.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.				
		5	10	30	60	120
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—
<i>B. dysenteriae</i>	do.....	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+

EXPERIMENT NO. 13.

Dilute formalin-permanganate method.

Formalin, 600 c. c.
Water, 300 c. c.
Permanganate, 375 grams.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Quantity of formaldehyde found per cubic foot, 0.03755 gram.
(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate, and consuming 34 minutes in the drawing.)
Yield of formaldehyde, 35.1 per cent.
Weather: Moderate breeze from west, few clouds.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	85	70	8.91
After 10 minutes.....	85	90	11.21
After 2 hours.....	85	82	10.43

See note, Experiment No. 9.
[+ means growth; – no growth.]

Organism.	How exposed.	Time of exposure in min- utes, and results.					
		5	10	25	30	60	120
<i>B. pyocyaneus</i>	Filter paper.....	–	–	–	–	–	–
<i>B. coli communis</i>	do.....	–	–	–	–	–	–
<i>B. dysenterix</i>	do.....	+	–	–	–	–	–
<i>B. subtilis</i>	do.....	+	+	+	+	–	–
<i>B. coli communis</i>	Wilson method.....	+	+	–	–	–	–
<i>B. subtilis</i>	do.....	+	+	+	+	+	–

EXPERIMENT NO. 14.

Dilute formalin-permanganate method.

Formalin, 600 c. c.
Water, 300 c. c.
Permanganate, 375 grams.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Quantity of formaldehyde found per cubic foot, 0.0341 gram.
(Determination made by drawing air from the room, beginning 17 minutes after mixing the formalin and permanganate, and consuming 42 minutes in the drawing.)
Yield of formaldehyde, 31.84 per cent.
Weather: Very light breeze, clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	85	70	8.91
After 10 minutes.....	85	88	11.21
After 2 hours.....	86	83	10.89

See note, Experiment No. 9.

EXPERIMENT NO. 14—Continued.

[+ means growth, — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	10	15	30	60	120
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—	—
<i>B. coli communis</i>do.....	—	—	—	—	—	—
<i>B. dysenterix</i>do.....	+	—	—	—	—	—
<i>B. subtilis</i>do.....	+	+	+	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—
<i>B. subtilis</i>do.....	+	+	+	+	—	—

The organisms were killed in the above experiment in about the same time as in those with the undiluted formalin-permanganate method under similar conditions of temperature and humidity.

The following two experiments (Nos. 14a and 14b), which were done after the room in experiment No. 14 had been left closed 4 and 24 hours, respectively, show how the percentage of formaldehyde became reduced by standing.

Although only 9.6 per cent of formaldehyde was found in experiment No. 14b, the organisms were killed within a comparatively short time. This demonstrates what a small percentage of formaldehyde will kill when the temperature and humidity are high. Under these conditions the principal effect of a limited reduction in the percentage of formaldehyde seems to be in decreasing penetration, as shown by results with exposures by the Wilson method.

EXPERIMENT NO. 14a.

After the room in experiment No. 14 had been left closed 4 hours.

Quantity of formaldehyde found per cubic foot, 0.02276 gram.

Yield of formaldehyde, 21.27 per cent.

Weather: Very gentle breeze during intervening 4 hours.

Temperature of room during experiment, 87° F.

Relative humidity, 79 per cent.

Absolute humidity, 10.69 grams per cubic foot.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	25	30	45	60	120
<i>B. pyocyaneus</i>	Filter paper.....	+	+	—	—	—	—	—
<i>B. coli communis</i>do.....	+	—	—	—	—	—	—
<i>B. dysenterix</i>do.....	+	+	—	—	—	—	—
<i>B. subtilis</i>do.....	—	—	—	—	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—	—
<i>B. subtilis</i>do.....	—	—	—	+	+	+	—

EXPERIMENT NO. 14b.

After the room in experiment No. 14 had been left closed 24 hours.

Quantity of formaldehyde found per cubic foot, 0.01028 gram.

Yield of formaldehyde, 9.6 per cent.

Weather: Gentle winds during intervening 24 hours.

Temperature of room during experiment, 84° F.

Relative humidity, 76 per cent.

Absolute humidity, 9.38 grams per cubic foot.

[+ means growth; - no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	25	30	45	60	120
<i>B. pyocyaneus</i>	Filter paper	+	+	-	-	-	-	-
<i>B. coli communis</i>	do.	+	-	-	-	-	-	-
<i>B. dysenterix</i>	do.	+	-	-	-	-	-	-
<i>B. subtilis</i>	do.	+	+	+	+	+	-	-
<i>B. coli communis</i>	Wilson method	+	+	+	-	-	-	-
<i>B. subtilis</i>	do.	+	+	+	+	+	+	-

EXPERIMENT NO. 15.

Dilute formalin-permanganate method.

Formalin, 600 c. c.

Water, 600 c. c.

Permanganate, 450 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 grams.

Quantity of formaldehyde found per cubic foot, 0.0279 gram.

(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate, and consuming 1 hour 20 minutes in the drawing.)

Yield of formaldehyde, 26.1 per cent.

Weather: Light east wind, clear.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	79.5	62	6.67
After 10 minutes	80.5	87	9.66
After 2 hours	81.0	81	9.13

See Note, Experiment 9.

[+ means growth; - no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	20	30	45	60	120
<i>B. coli communis</i>	Glass	-	-	-	-	-	-	-
<i>B. subtilis</i>	do.	+	+	+	+	+	+	+
<i>B. pyocyaneus</i>	Filter paper	+	-	-	-	-	-	-
<i>B. typhosus</i>	do.	+	-	-	-	-	-	-
<i>B. subtilis</i>	do.	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method	+	+	-	-	-	-	-

Although the relative humidity in the above experiment was 62 per cent and the temperature 79.5° F., the spores of *B. subtilis* were not killed within two hours; this was due in all probability to the humidity being insufficient. The other organisms were killed within a few minutes. The humidity was increased 25 per cent by the moisture given off, but this did not seem to answer the purpose in case of the spores.

The following two experiments (Nos. 16 and 17) were done during colder weather than the foregoing. The results show a marked decrease in the percentage of formaldehyde obtained, as well as diminished germicidal powers. About the same hazy appearance in the room was observed as with the undiluted formalin-permanganate method under similar conditions of temperature, but the deposit of paraform was not so marked.

Comparing experiments Nos. 7 and 8 (undiluted formalin-permanganate) with Nos. 16 and 17 it will be observed that, although the temperature was lower in the latter experiments than in the former, the germicidal results are in favor of the latter experiments.

EXPERIMENT NO. 16.

Dilute formalin-permanganate method.

Formalin, 600 c. c.

Water, 300 c. c.

Permanganate, 375 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.01626 gram.

(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate, and consuming 1 hour 5 minutes in the drawing.)

Yield of formaldehyde, 15.2 per cent.

Weather: Light clouds, northwest breeze.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	39	51	1.39
After 10 minutes.....	42	92	2.82
After 3 hours.....	40	83	2.36

See Note, Experiment No. 9.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.							
		10	20	30	45	60	90	120	180
<i>B. coli communis</i>	Filter paper.....	+	—	—	—	—	—	—	—
<i>B. typhosus</i>	do.....	+	—	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+	+	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+	+

EXPERIMENT NO. 17.

Dilute formalin-permanganate method.

Formalin, 600 c. c.

Water, 600 c. c.

Permanganate, 450 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.01234 gram.

(Determination made by drawing air from the room, beginning 15 minutes after mixing the formalin and permanganate, and consuming 1 hour 30 minutes in the drawing.)

Yield of formaldehyde, 11.53 per cent.

Weather: Cloudy, north wind.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing HCHO and KMnO ₄	41	55	1.62
After 10 minutes	40	92	2.51
After 3 hours	41.5	61	1.83

See Note, Experiment No. 9.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and result.						
		10	20	30	45	60	90	180
<i>B. coli communis</i>	Filter paper	+	—	—	—	—	—	—
<i>B. typhosus</i>do	+	—	—	—	—	—	—
<i>B. subtilis</i>do	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method	+	+	+	+	+	+	+
<i>B. subtilis</i>do	+	+	+	+	+	+	+

For practical disinfection purposes the results of the undiluted and diluted formalin-permanganate methods do not, on the whole, differ materially. The relative humidity is increased in about the same proportions in the two methods and the organisms killed in about the same time. The only advantage in diluting the formalin seems to be when working at a reduced temperature. Then polymerization does not seem to take place as much as when the water is not added. This may account for the relatively larger percentage yield of formaldehyde, as well as its more efficient germicidal action in experiments Nos. 16 and 17 as compared with experiments Nos. 7 and 8.

Comparing experiment No. 16, in which 300 c. c. of water were added, with experiment No. 17, in which 600 c. c. of water were added, it will be seen that the addition of the former quantity of water gave slightly better germicidal results than the latter. This would indicate that there is nothing to be gained by diluting the quantity of formalin with more than half its volume of water. This statement, however, must not be construed as recommending the diluted formalin-permanganate method for disinfection purposes

during cold weather, but simply as showing that under these conditions it possesses a slight advantage over the undiluted formalin-permanganate method.

Except under the conditions as stated, the addition of the water is a disadvantage, as the percentage of formaldehyde liberated is diminished in proportion to the quantity of water used, and, furthermore, a larger quantity of permanganate is required.

III. RETORT WITHOUT PRESSURE.^a

The formalin in this method is simply heated to the boiling point under atmospheric pressure in a retort, and the issuing water vapor and formaldehyde gas are passed into the room through a suitable tube.

In the following experiments 600 c. c. of formalin, to which were added 6 c. c. of glycerine, were taken for the charge, and the heat was continued under the retort until vapor practically ceased to issue from the outlet tube.

When the retort was removed, there was practically no liquid left in it. The time required to vaporize the formalin varied from 1 hour to 1 hour and 10 minutes in the different experiments, depending upon the degree of the temperature.

Chemical determinations.—These determinations were made by drawing air from the room, beginning usually a short time after exhausting the retort; however, two were made after waiting 3 hours and 40 minutes, and 72 hours, respectively. The method of procedure has been described, page 11.

The results are shown in the following table:

TABLE 3.—*Experiments with the retort without pressure.*

Number.	Temperature of room before experiment.	Time required to exhaust retort.	Time between removal of retort and drawing air.	Time required to draw air.	Volume of air drawn, in liters.	Relative humidity before experiment.	Relative humidity at end of injection.	Increase in grains of moisture per cubic foot.	Abs. formaldehyde used per cubic foot.	Abs. formaldehyde found per cubic foot.	Per cent yield.	Condition of wind.
I	° F. 73	<i>h. m.</i> 1 0	<i>h. m.</i> 0 22	<i>h. m.</i> 1 6	10	73	86	1.5	<i>gm.</i> 0.107	<i>gm.</i> 0.05037	47.07	Very slight breeze.
II ^a	76	1 0	0 21	1 10	10	82	89	0.96	.107	.04935	46.12	Do.
II ^b			3 40	1 4	8	-----	-----	-----	.107	.04183	39.1	Do.
II ^c			72 0	1 7	10	-----	-----	-----	.107	.00637	5.95	Strong wind July 29, 30, 31.
III	40	1 10	0 15	1 20	12	52	69	.67	.107	.01982	18.4	Light wind.

^a The retort used is the Trenner-Lee formaldehyde disinfecter, manufactured by J. Ellwood Lee Company, Conshohocken, Pa.

With comparatively high temperatures, say, 75° F., the yield of formaldehyde gas by this method was appreciably higher than by the autoclave method, although the time required to exhaust the apparatus was more than twice as long in the former than in the latter. Because of this longer time there was naturally more loss by leakage in the retort method before beginning to draw air. The higher percentage would be expected, since in the retort the formaldehyde is not subjected to so high a temperature and pressure as in the autoclave.

Experiment II *c* shows the loss by leakage after the room in experiment II had been left closed 72 hours. Although the yield was greater in the retort than by any other method tried, there arises the question, What becomes of the rest of the formaldehyde? This point is an interesting one and worthy of further investigation, but will not be taken up in this work except in so far as a reduction in temperature affects the percentage of formaldehyde obtained. This reduction is shown in experiment III (temperature 40° F.,) in which only 18.4 per cent was obtained as against 46.12 per cent in experiment II (temperature 73° F.)

A slightly lower temperature with this method seems necessary to produce the same appearance in the room that is observed in the undiluted formalin-permanganate method; that is, about 55° F. with this method as against 60° to 65° F. with the method referred to. Even then the deposit of paraform is not so marked as with the undiluted formalin-permanganate method. The reason for this is not apparent, since the percentages obtained with the two methods showed about the same relative decrease.

The quantity of paraform deposited in the room is about the same with this method as with the diluted formalin-permanganate and autoclave methods.

Germicidal properties.—As it took approximately 1 hour to exhaust the quantity of formalin used in these experiments, the organisms were not exposed to the action of the formaldehyde until this process was completed. The organisms were prepared and exposed in the usual manner previously described.

A summary of conditions and results is given in each of the following experiments:

EXPERIMENT NO. 18.

Retort without pressure.

Formalin, 600 c. c.; glycerin, 6 c. c.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Time required to exhaust material in retort, 1 hour.
Quantity of formaldehyde found per cubic foot, 0.05037 gram.
(Determination made by drawing air from room, beginning 22 minutes after exhausting retort and consuming 1 hour 6 minutes in the drawing.)
Yield of formaldehyde, 47.07 per cent.
Weather: Slight wind southwest, cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	73.5	73	6.40
After 1 hour.....	74.5	86	7.91
After 2 hours.....	75.0	86	8.00

NOTE.—In all the experiments with this method the temperature and humidity are given from the time of beginning to introduce the gas. The organisms were exposed immediately after exhausting the retort.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in min- utes, and results.					
		2	5	10	20	30	60
<i>B. pyocyaneus</i>	Filter paper.....	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—	—
<i>B. dysenterix</i>	do.....	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—

EXPERIMENT NO. 19.

Retort without pressure.

Formalin, 600 c. c.; glycerin, 6 c. c.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Time required to exhaust material in retort, 1 hour.
Percentage yield of formaldehyde undetermined.
Weather: Slight westerly wind, clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	74.5	60	5.52
After 1 hour.....	75.0	84	7.85
After 2 hours.....	75.0	82	7.66

See note, Experiment No. 18.

EXPERIMENT NO. 19—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		2	5	10	20	30	60
<i>B. pyocyaneus</i>	Filter paper.....	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—	—
<i>B. dysenterix</i>	do.....	+	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—

EXPERIMENT NO. 20.

Retort without pressure.

Formalin, 600 c. c.; glycerin, 6 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Time required to exhaust material in retort, 1 hour.

Quantity of formaldehyde found per cubic foot, 0.04708 gram.

(Determination made by drawing air from room beginning 25 minutes after exhausting retort and consuming 1 hour 20 minutes in the drawing.)

Yield of formaldehyde, 44 per cent.

Weather: Rather strong northwest wind; clear.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	74	74	6.70
After 1 hour.....	75	84	7.85
After 2 hours.....	74	89	8.06

See Note, experiment No. 18.

[+ means growth; — no growth].

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	10	20	30	45	60
<i>B. pyocyaneus</i>	Filter paper.....	—	—	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—	—
<i>B. dysenterix</i>	do.....	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	0	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—	—

EXPERIMENT NO. 21.

Retort without pressure.

Formalin, 600 c. c.; glycerin, 6 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Time required to exhaust material in retort, 1 hour.

Quantity of formaldehyde found per cubic foot, 0.04935 gram.

(Determination made by drawing air from room, beginning 21 minutes after exhausting retort and consuming 1 hour 10 minutes in the drawing.)

Yield of formaldehyde, 46.12 per cent.

Weather: Light westerly wind; cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	76	82	7.91
After 1 hour.....	77	89	8.87
After 2 hours.....	77	89	8.87

See Note, experiment No. 18.

[+ means growth; — no growth].

Organism.	How exposed.	Time of exposure in minutes, and results.				
		2	5	10	25	60
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—
<i>B. dysenterix</i>	do.....	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—

For surface disinfection better results could not be desired than were obtained in the above experiments. The temperature and humidity being comparatively high, the nonspore-bearing organisms were killed within five to ten minutes and the spores of *B. subtilis* within one hour, the time varying slightly in the different experiments.

Although the humidity in experiment No. 19 was only 60 per cent before starting, the results are about as good as in those in which the humidity was considerably higher.

In the following experiment (No. 21^a) which was done after the room in experiment No. 21 had been left closed 72 hours (3 days), only 5.95 per cent of formaldehyde was found. Still *B. pyocyaneus* and *B. coli communis* exposed on filter paper were killed within 1 hour and *B. dysenterix* within 30 minutes. This shows, as has been previously mentioned, what a small percentage of formaldehyde will kill nonspore-bearing organisms when we have proper temperature and humidity. The spores of *B. subtilis* were not killed within 2 hours.

EXPERIMENT NO. 21a.

After the room in experiment No. 21 had been left closed 72 hours (3 days).

Quantity of formaldehyde found per cubic foot, 0.00637 gram.

Yield of formaldehyde, 5.95 per cent.

Weather: Rather strong wind during the 3 days; rained several times.

Temperature of room during experiment, 75° F.

Relative humidity, 78 per cent.

Absolute humidity, 7.30 grams per cubic foot.

[+ means growth; - no growth].

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	10	20	30	60	120
<i>B. pyocyaneus</i>	Filter paper.....	+	+	+	+	-	-
<i>B. coli communis</i>do.....	+	+	+	+	-	-
<i>B. dysenteriae</i>do.....	+	+	+	-	-	-
<i>B. subtilis</i>do.....	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+

The following experiment (No. 22) was done at a comparatively low temperature, in consequence of which the percentage of formaldehyde gas obtained was small. The same hazy appearance of the air in the room was observed as with the previous methods under similar conditions of temperature. The deposit of paraform was not so marked as with the undiluted formalin-permanganate method, but about the same as with the diluted method.

Considering the difference in temperature, the germicidal action of the formaldehyde in this experiment is better than in experiment No. 8 with the formalin-permanganate method.

EXPERIMENT NO. 22.

Retort without pressure

Formalin, 600 c. c.; glycerin, 6 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Time required to exhaust material in retort, 1 hour and 10 minutes..

Quantity of formaldehyde found per cubic foot, 0.01982 gram.

(Determination made by drawing air from room, beginning 15 minutes after exhausting retort and consuming 1 hour and 20 minutes in the drawing).

Yield of formaldehyde. 18.4 per cent.

Air in room had a very hazy appearance during the experiment, probably due to polymerization of formaldehyde.

Weather: Clear and cold; light northeast wind.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	40	52	1.47
After 1 hour.....	42	69	2.11

See Note, Experiment No. 18.

EXPERIMENT NO. 22—Continued.

[+ means growth; — no growth].

Organism.	How exposed.	Time of exposure in minutes, and results.						
		10	20	30	45	60	120	180
<i>B. typhosus</i>	Filter paper.....	+	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+

What has been said in regard to temperature, humidity, and percentage of formaldehyde with the formalin-permanganate method practically applies to this method also. This method might be employed when the temperature is a few degrees lower than is permissible with the formalin-permanganate method; but the difference is not sufficient to be of much practical importance. Apparently polymerization does not take place quite so markedly, but about the same comparative reductions in the percentage of formaldehyde obtained are observed with the two methods when the temperature is low.

The time required to destroy microorganic life is about the same in the two methods. The principal objections to the retort method are that special apparatus is required and considerable time is consumed in vaporizing the formalin.

IV. THE AUTOCLAVE UNDER PRESSURE.^a

Six hundred c. c. of formalin, 60 c. c. of glycerin, 120 gm. of calcium chlorid, and water sufficient to make a volume of 1,000 c. c. constituted the charge for each experiment. The pressure was raised to between 50 and 60 pounds, when the cock was opened and injection continued till the pressure had fallen to about 40 pounds. Then the pressure was raised and vapor again injected.

This process was repeated until the pressure arose very slowly and vapor ceased to escape from the nozzle of the autoclave, which was inserted through a suitable hole in the door. After each experiment there was very little liquid left in the autoclave.

The time required to vaporize the quantity of formalin, etc., used varied from 22 to 28 minutes in the different experiments, depending upon the temperature of the atmosphere.

Chemical determinations.—The method of procedure has been described.

The results are shown in the following table:

^aThe one used is the Kinyoun-Francis autoclave, manufactured by the Kensington Engine Works (Limited), Philadelphia, Pa.

TABLE 4.—*Experiments with the autoclave.*

Number.	Temperature of room before experiment.	Time required to exhaust autoclave.	Time between beginning of discharge to drawing of air.	Time required to draw air.	Volume of air drawn, in liters.	Relative humidity before experiment.	Relative humidity 5 minutes after removing autoclave.	Increase in grains of moisture per cubic foot.	Abs. formaldehyde used per cubic foot.	Abs. formaldehyde found per cubic foot.	Per cent yield.	Weather conditions.
	° F.	m.	h. m.	h. m.					gm.	gm.		
I	80	25	3 32	1 18	10	75	96	2.96	0.107	0.0406	37.94	Almost no wind.
II	31.5	25	a 35 b 3 33	1 17 1 4	10 10	81	94	2.00107 .107	0.04213 0.0216	39.37 20.18	Good breeze. Storm.
III	80	22	a 40 b 1 41	1 10 1 20	11 11	75	94	2.23107 .107	0.04448 0.04116	41.57 38.46	Almost no wind. Do.
IV	49	25	0 15	1 7	10	67	81	.78	.107	0.1851	17.30	No wind.
V	41	23	0 15	1 30	10	69	92	.77	.107	0.01471	13.75	Light breeze.

From the result of III *a* it seems probable that on a warm calm day in a fairly tight room the amount of formaldehyde by the autoclave from 600 c. c. of formalin would be approximately 42 per cent after an interval of about 15 minutes from the time of removing the nozzle from the room.

II *a* is lower than III *a*, which was to be expected, because of the strong wind.

II *b* shows the rapid loss of formaldehyde gas during a strong wind or storm. During the time that the air was drawn in this experiment a severe windstorm was in progress, with the result that during the interval of 3 hours between *a* and *b* nearly half the formaldehyde escaped from the room.

In these, as in the determinations in the case of the other methods of charging the room, the results represent the average quantity of formaldehyde for the interval during which the air was drawn.

Even during warm weather (80° F.) apparently over half of the formaldehyde gas in the 600 c. c. of formalin used to charge the room was lost. It is altogether improbable that the most of this escaped from the room during the 25 minutes required to exhaust the autoclave, as is evident from the slow rate of loss on a calm day shown in I and III *a* and *b*. It is more probable that under the high temperature and pressure in the autoclave the formaldehyde undergoes change. The effects of a reduced temperature upon formaldehyde liberated by this method were about the same as those observed in case of the other methods already described. The reduction in percentage of formaldehyde obtained is shown in experiments IV, temperature 49° F., and V, temperature 41° F., which gave 17.30 per cent and 13.75 per cent, respectively.

Germicidal properties.—The method of procedure has been described, the organisms being exposed after all the formalin, etc., had been vaporized and injected.

The following are the conditions and results of the different experiments.

EXPERIMENT NO. 23.

Autoclave.

Formalin, 600 c. c.; glycerin, 60 c. c.; calcium chloride, 120 grams; water sufficient to make 1,000 c. c.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Time required to exhaust material in autoclave, 25 minutes.
Quantity formaldehyde found per cubic foot, 0.04213 gram.
(Determination made by drawing air from room beginning 35 minutes after exhausting autoclave and consuming 1 hour 17 minutes in the drawing.)
Yield of formaldehyde, 39.37 per cent.
Weather: Moderate westerly wind; cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	81.5	81	9.26
After 30 minutes.....	83.0	94	11.26
After 2 hours.....	82.0	86	10.00

NOTE.—In all the experiments with this method the temperature and humidity are given from the time of beginning to introduce the gas; the organisms were exposed immediately after exhausting the autoclave.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		2	5	10	20	30	60
<i>B. coli communis</i> *.....	Glass.....	+	—	—	—	—	—
<i>B. pyocyaneus</i>	Filter paper.....	+	+	—	—	—	—
<i>B. typhosus</i>do.....	+	—	—	—	—	—
<i>B. coli communis</i>do.....	+	+	—	—	—	—
<i>B. dysenterix</i>do.....	+	+	—	—	—	—
<i>B. subtilis</i>do.....	—	—	—	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—

EXPERIMENT NO. 24.

Autoclave.

Formalin, 600 c. c.; glycerin, 60 c. c.; calcium chloride, 120 grams; water sufficient to make 1,000 c. c.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Time required to exhaust material in autoclave, 25 minutes.
Quantity formaldehyde found per cubic foot, 0.0406 gram.
(Determination made by drawing air from room beginning 3 hours 32 minutes after exhausting autoclave and consuming 1 hour 18 minutes in the drawing.)
Yield of formaldehyde, 37.94 per cent.
Weather: Practically no wind; cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	80	75	8.20
After 30 minutes.....	82	96	11.16
After 2 hours.....	81	91	10.58

See Note, Experiment No. 23.

EXPERIMENT NO. 24—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		2	5	10	20	30	60
<i>B. coli communis</i>	Glass.....	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	—	—	—	—	—	—
<i>B. pyocyaneus</i>	Filter paper.....	+	—	—	—	—	—
<i>B. typhosus</i>	do.....	+	—	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	—	—	—	—	—	—

EXPERIMENT NO. 25.

Autoclave.

Formalin, 600 c. c.; glycerin, 60 c. c.; calcium chloride, 120 grams; water sufficient to make 1,000-c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Time required to exhaust material in autoclave, 22 minutes.

Quantity formaldehyde found per cubic foot, 0.04448 gram.

(Determination made by drawing air from room, beginning 40 minutes after exhausting autoclave, and consuming 1 hour 10 minutes in the drawing.)

Yield of formaldehyde, 41.57 per cent.

Weather: Slight westerly breeze.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	80.0	75	8.20
After 30 minutes.....	80.5	94	10.43
After 2 hours.....	81.0	94	10.59

See Note, experiment No. 23.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		2	5	10	20	30	60
<i>B. pyocyaneus</i>	Filter paper.....	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—	—
<i>B. dysenterix</i>	do.....	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	—	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—

The above experiments show very efficient germicidal results. Even the spores of *B. subtilis* exposed by the Wilson method were killed within 10 minutes in experiments Nos. 23 and 24.

In experiment No. 25 the time required to kill the different organisms was prolonged as compared with the two previous experiments;

this was especially so with the spores of *B. subtilis* exposed by the Wilson method. The reason for this is not apparent, since the temperature and humidity were practically the same in the different experiments.

In the following experiment (No. 26) the germicidal power of the formaldehyde was much diminished as a result of the low humidity—46 per cent—before starting the experiment.

EXPERIMENT NO. 26.

Autoclave.

Formalin, 600 c. c.; glycerin, 60 c. c.; calcium chloride, 120 grams; water sufficient to make 1,000 c. c.
Capacity of room, 2,000 cubic feet.
Quantity of formaldehyde used per cubic foot, 0.107 gram.
Time required to exhaust material in autoclave, 22 minutes.
Yield of formaldehyde, undetermined.
Weather: Rather strong westerly wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	68	46	3.45
After 30 minutes.....	69	67	5.17
After 2 hours.....	69	60	4.63

See Note, experiment No. 23.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in min- utes, and results.						
		5	15	30	45	60	120	180
<i>B. pyocyaneus</i>	Glass.....	+	+	+	+	—	—
<i>B. typhosus</i>do.....	+	+	+	—	—	—
<i>B. staph. py. aureus</i>do.....	+	+	+	+	—	—
<i>B. coli communis</i>do.....	+	+	+	+	—	—
<i>B. pyocyaneus</i>	Filter paper.....	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+

When working at reduced temperatures the same decrease in percentage yield of formaldehyde and the same deficiency in germicidal action are observed in this method as in the formalin-permanganate and the retort methods. This is shown in the following two experiments, in which the spores of *B. subtilis* were not usually killed within 3 hours, although the nonspore-bearing organisms exposed directly on slips of filter paper were killed in a fairly short time.

Comparing the results of these two experiments with experiment No. 26, it will be seen that a reduction in humidity diminishes the killing power of formaldehyde more than does a similar reduction in temperature.

EXPERIMENT NO. 27.

Autoclave.

Formalin, 600 c. c.; glycerin, 60 c. c.; calcium chloride, 120 grams; water sufficient to make 1,000 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Time required to exhaust material in autoclave, 25 minutes.

Quantity formaldehyde found per cubic foot, 0.01851 gram.

(Determination made by drawing air from room, beginning 15 minutes after exhausting autoclave, and consuming 1 hour 7 minutes in the drawing.)

Yield of formaldehyde, 17.30 per cent.

Weather: Very little wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	49	67	2.63
After 30 minutes.....	51	81	3.41
After 2 hours.....	54	61	2.85

See Note, experiment No. 23.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		10	20	30	45	60	120	180
<i>B. coli communis</i>	Filter paper.....	+	—	—	—	—	—	—
<i>B. typhosus</i>	do.....	—	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+

EXPERIMENT NO. 27.

Autoclave.

Formalin 600 c. c., glycerin 60 c. c., calcium chloride 120 grams, water sufficient to make 1,000 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Time required to exhaust material in autoclave, 28 minutes.

Quantity formaldehyde found per cubic foot, 0.01471 gram.

(Determination made by drawing air from room, beginning 15 minutes after exhausting autoclave and consuming 1 hour 30 minutes in the drawing.)

Yield of formaldehyde, 13.75 per cent.

Weather: Damp and snow on ground; light wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before beginning to introduce the gas.....	41	69	2.04
After 30 minutes.....	42	92	2.81
After 2 hours.....	42	84	2.57

See Note, Experiment No. 23.

EXPERIMENT NO. 27—Continued.

[+ means growth, — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		10	20	30	45	60	120	180
<i>B. coli communis</i>	Filter paper.....	+	+	—	—	—	—	—
<i>B. typhosus</i>	do.....	+	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+

These results agree rather closely with those of the formalin-permanganate and retort methods and especially with the latter method, except that the retort liberates a slightly larger percentage of formaldehyde than does the autoclave. For disinfecting purposes the three methods give about the same results, provided the temperature and humidity are high. A low temperature affects the autoclave method in about the same way that it does the retort method. The disadvantages of the autoclave are that more or less complicated apparatus is required which is cumbersome to handle and that considerable time is consumed in vaporizing the formalin, although not half so long as with the retort.

V. SHEET-SPRAYING METHOD.

Two sheets, about $4\frac{1}{2}$ by $6\frac{1}{2}$ feet, were hung up in the room in a slanting position at an angle of about 45° . It was found advantageous to have them just damp to the touch when hung up, as the formalin was absorbed by the fibers more quickly and had very little tendency to run off the sheet. Six hundred c. c. of formalin were sprayed uniformly and the door closed.

Chemical determinations.—Different intervals were allowed to elapse after spraying the sheets before beginning to draw air from the room. The method of procedure has been described. The results are given in the following table:

TABLE 5.—Experiments with the sheet-spraying method.

Number.	Temperature of room before experiment.	Time between closing room and drawing air.		Time required to draw air.	Volume of air drawn, in liters.	Relative humidity before experiment.	Relative humidity after closing room.	Gain in grains of moisture per cubic foot.	Abs. formaldehyde used per cubic foot.	Abs. formaldehyde found per cubic foot.	Per cent.	Condition of wind
	° F.	h.	m.	h. m.					Gm.	Gm.		
Ia	76.5	1	26	1 13	10	72	a 83	1.6	0.107	0.02576	24.07	No wind.
Ib		3	47	1 8	10107	.03262	30.48	Do.
IIa	78	1	40	1 15	10	3	b 85107	.0252	23.55	Gentle breeze.
IIb		4	5	1 7	10107	.0305	28.50	Do.
IIc		23	30	1 17	10107	.02225	20.80	No wind.
III	43.5	1	30	1 25	11	52	61	0.05	.107	.00345	3.16	Gentle breeze.

^a After 5 hours.^b After 3 hours.

Compared with the previous methods this one produces a fairly large quantity of formaldehyde gas in the air of the room when used during warm weather, say at a temperature of 75° F. The results under these conditions show that the quantity increases during a relatively long period of time. In experiment II *c*, Table 5, the quantity of formaldehyde gas found after an interval of 22 hours was only 2.75 per cent less than that found in II *a*, 90 minutes after closing the room. During cold weather, say temperature of 43.5° F., very little formaldehyde is liberated, as the result of experiment III shows. Evaporation takes place very slowly and the formalin polymerizes on the sheets.

Germicidal properties.—In these experiments the organisms were prepared and exposed in the usual way, but not until one hour after spraying. This allowed time for at least a portion of the formaldehyde to be given off and become diffused.

A summary of conditions and results is given in each of the following experiments:

EXPERIMENT NO. 28.

Sheet spraying.

Formalin, 600 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.02576 gram.

(Determinations made by drawing air from room beginning 1 hour 26 minutes after spraying sheets and consuming 1 hour 15 minutes in the drawing.)

Yield of formaldehyde, 24.07 per cent.

Condition of weather: Very light wind, slightly cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before spraying.....	76.5	72	7.05
1 hour after.....	76.0	80	7.72
2 hours after.....	77.0	81	8.06

Organisms not exposed until 1 hour after spraying sheet.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	20	30	60	90	120
<i>B. pyocyaneus</i>	Filter paper.....	+	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—	—	—
Do.....	Wilson method.....	+	+	+	—	—	—	—
<i>B. dysenteriae</i>	Filter paper.....	+	+	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—	—	—
Do.....	Wilson method.....	+	+	+	+	+	—	—

EXPERIMENT NO. 29.

Sheet spraying.

Formalin, 600 c. c.

Capacity of room, 2,000 cubic feet.

Percentage of formaldehyde liberated was not determined.

Condition of weather: Light northwest wind, clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before spraying.....	74.0	80	7.25
1 hour after.....	74.5	86	7.91
2 hours after.....	76.0	89	8.6

Organisms not exposed until 1 hour after spraying sheets.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	20	30	60	90	120
<i>B. pyocyaneus</i>	Filter paper.....		+	+	—	—	—	—
<i>B. coli communis</i>do.....		+	—	—	—	—	—
Do.....	Wilson method.....		+	+	+	—	—	—
<i>B. dysenteriz</i>	Filter paper.....		+	—	—	—	—	—
<i>B. subtilis</i>do.....		+	+	+	—	—	—
Do.....	Wilson method.....		+	+	+	+	+	—

EXPERIMENT NO. 30.

Sheet spraying.

Formalin, 600 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.0252 gram.

(Determinations made by drawing air from room beginning 1 hour 40 minutes after spraying sheets and consuming 1 hour 15 minutes in the drawing.)

Yield of formaldehyde, 23.55 per cent.

Condition of weather: Light southerly wind, light clouds.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before spraying.....	78	83	8.52
1 hour after.....	77	87	8.67
2 hours after.....	79	85	9.01

Organisms not exposed until 1 hour after spraying sheets.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes and results.						
		5	10	20	30	60	90	120
<i>B. pyocyaneus</i>	Filter paper.....		—	—	—	—	—	—
<i>B. coli communis</i>do.....		—	—	—	—	—	—
Do.....	Wilson method.....		+	+	—	—	—	—
<i>B. dysenteriz</i>	Filter paper.....		—	—	—	—	—	—
<i>B. subtilis</i>do.....		—	—	—	—	—	—
Do.....	Wilson method.....		+	+	+	+	—	—
<i>B. dysenteriz</i>do.....		+	—	—	—	—	—

EXPERIMENT NO. 30 *a*.

After the room in experiment No. 30 had been left closed 24 hours.

Quantity of formaldehyde found per cubic foot, 0.02225 gram.

Yield of formaldehyde, 20.80 per cent.

Weather: No wind.

Temperature, 72° F.

Relative humidity, 91 per cent.

Absolute humidity, 8.51 per cubic feet.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		5	10	20	30	60	90	120
<i>B. pyocyaneus</i>	Filter paper.....	—	—	—	—	—	—	—
<i>B. coli communis</i>	do.....	—	—	—	—	—	—	—
Do.....	Wilson method.....	+	—	—	—	—	—	—
<i>B. dysenterix</i>	Filter paper.....	—	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	—	—	—	—	—	—	—
Do.....	Wilson method.....	+	+	+	+	—	—	—

The exposed organisms were killed in the above experiments in a comparatively short time, but hardly as short as in the previous methods under similar conditions of temperature and humidity.

Experiment No. 30 *a* was tried after the room in experiment No. 30 had been left closed 24 hours. It shows that in a well-closed room like the one used by us the percentage of formaldehyde gas in the room was still comparatively high after 24 hours' standing and that the exposed organisms were killed then in about the same time that they were 1 hour after spraying the sheets.

The following experiment (No. 31) shows the inefficiency of this method for disinfection purposes during cold weather, temperature 43.5° F. In this experiment even the nonspore-bearing organisms were not killed within 3 hours and only 3.16 per cent of formaldehyde was found.

EXPERIMENT NO. 31.

Sheet spraying.

Formalin, 600 c. c.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyhde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.00345 gram.

(Determinations made by drawing air from room beginning 1 hour 30 minutes after spraying sheets and consuming 1 hour 15 minutes in the drawing.)

Yield of formaldehyde, 3.16 per cent.

Condition of weather: Clear and dry, light southwesterly breeze.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before spraying.....	43.5	52	1.67
1 hour after.....	43.0	55	1.74
3 hours after.....	50.0	61	2.48

Organisms not exposed until 1 hour after spraying sheets.

EXPERIMENT NO. 31—Continued.

[+ means growth; — no growth.]

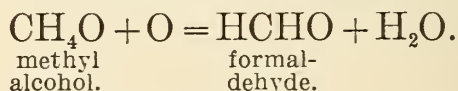
Organism.	How exposed.	Time of exposure in minutes, and results.					
		15	30	45	60	120	180
<i>B. coli communis</i>	Filter paper.....	+	+	+	+	+	+
<i>B. typhosus</i>do.....	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+

This method is very reliable for surface disinfection during warm weather provided the sheets are properly sprayed. Not over 300 c. c. of formalin should be used for every 30 square feet of sheet surface. The percentage of formaldehyde remains comparatively high during a relatively long time. The maximum of 30 per cent seems to be reached after approximately 4 hours standing, but at the end of 24 hours, 20.8 per cent was still found.

This is quite different from the other methods in which the percentage of formaldehyde begins to diminish by leakage from the moment the charging is finished. Evaporation maintains the humidity at a fairly high percentage which, with the constancy of liberation of formaldehyde, makes the method very applicable when a large exposure is required. On the other hand the influence of a low temperature upon the results obtained with this method is more marked than with any other methods tried. It was found that at a temperature of 43.5° F. very little formaldehyde is liberated and that the formalin gradually polymerizes on the sheets. This of course makes the use of this method for disinfection purposes absolutely impracticable during cold weather.

VI. THE GENERATING LAMP.^a

The lamp used in this work is one of the various lamps devised for the purpose of generating formaldehyde by oxidation of methyl alcohol. This is brought about by means of incandescent platinized asbestos, which has the power of causing the oxygen of the air and methyl alcohol vapor to combine according to the following reaction:



The platinized asbestos is heated by first burning some of the alcohol, after which the flame is extinguished. Alcohol continues to vaporize and the heat produced in the oxidation maintains the temperature of the apparatus. The time usually allowed for the exhaustion of the lamp is about 2 hours.

^a The lamp used is manufactured by the Kuhn Formaldehyde Generator Co., Alexandria, Va.

One thousand c. c. of commercial methyl alcohol were placed in the reservoir of the lamp and 1,500 c. c. of water in the basin around the reservoir.

In a preliminary experiment it was found necessary to have two silver nitrate tubes to absorb the hydrocyanic acid which was carried over from the cyanide absorption tubes by the air bubbling through them. This was no doubt due to the presence of a relatively large amount of carbonic acid and perhaps a small quantity of formic acid.

While formaldehyde is formed by the action of the platinized asbestos in the lamp, it is more than likely that it is not the only product of oxidation, but that the oxidation extends as far as the formation of carbonic acid. It is known that formic acid is oxidized to carbonic acid by platinized asbestos. The presence of either carbonic or formic acid in the air bubbling through the cyanide absorption tubes would cause the liberation of some hydrocyanic acid, which would be carried over. The precipitate in the first silver nitrate tube was somewhat greater than in the case of the other methods. The precipitate in the second silver nitrate tube did not appear until toward the end of the experiment.

The chemical determinations were made as follows:

I. Began to draw air 2 hours after lamp was started; volume of air drawn, 10 liters; time required, 1 hour 13 minutes; condition of wind, gentle breeze.

Temperature of room before experiment, 79° F.; relative humidity, 87 per cent.

Temperature of room 2 hours after starting lamp, 85° F.; relative humidity, 98 per cent.

Formaldehyde found per cubic foot, 0.01096 gram.

II. Began to draw air 2 hours after starting lamp; volume of air drawn, 10 liters; time required, 1 hour 6 minutes; condition of wind, moderate breeze.

Temperature of room before experiment, 75° F.; relative humidity, 82 per cent.

Temperature of room 2 hours after starting lamp, 92° F.; relative humidity, 96 per cent.

Formaldehyde found per cubic foot, 0.00986 gram.

In another experiment, which was done during colder weather than the above, the following are the results:

III. Began to draw air 2 hours after starting lamp; volume of air drawn, 10 liters; time required, 1 hour 15 minutes; condition of wind; light breeze.

Temperature of room before experiment, 42° F.; relative humidity, 69 per cent.

Temperature of room 2 hours after starting lamp, 49° F.; relative humidity, 86 per cent.

Formaldehyde found per cubic foot, 0.00424 gram.

As the formaldehyde is derived from methyl alcohol it is impossible to make a comparison of the percentages of formaldehyde obtained by this method with those obtained by the other methods in which formalin is used instead of alcohol.

Germicidal properties.—In all but two of the experiments the organisms were placed in the wire trays in the room before the lamp was started and the time of exposure estimated from the moment of starting the lamp and closing the room. This appeared to be the most rational way of estimating the time of exposure, as the lamp was in

the room and it was impossible to determine the time at which the process of evolving the gas was completed. The room was not closed until it was found that the formaldehyde gas was being given off by the lamp. This was detected by its irritating action on the mucous membrane of the eyes and nose. However, in two experiments the exposures were made 2 hours after starting the lamp and closing the room.

A summary of conditions and results is given in each of the following experiments:

EXPERIMENT NO. 32.

Generating lamp.

Methyl alcohol, 1,000 c. c.^a
Capacity of room, 2,000 cubic feet.
Weather: No wind, slightly cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before starting lamp.....	73	82	7.20
After 1 hour.....	81	85	9.58
After 2 hours.....	81	98	11.05
After 3 hours.....	79	98	11.05

Time of exposure of organisms counted from time of starting the lamp.

[+ means growth; —, no growth.]

Organism.	How exposed.	Time of exposure in minutes and results.						
		10	20	30	45	60	120	180
<i>B. coli communis</i>	Glass.....	+	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—	—
<i>B. pyocyaneus</i>	Filter paper.....	+	+	+	—	—	—	—
<i>B. typhosus</i>	do.....	+	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	—	—

^a For a room of this size the United States Quarantine regulations require 1,400 c. c. of methyl alcohol.

EXPERIMENT NO. 33.

Generating lamp

* Methyl alcohol, 1,000 c. c.
Capacity of room, 2,000 cubic feet.
Weather: Light southwest wind, clear.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before starting lamp.....	79	87	9.23
After 1 hour.....	86	88	11.35
After 2 hours.....	85	98	12.48
After 3 hours.....	84	98	12.11

Time of exposure of organisms counted from time of starting the lamp.

[+means growth; - no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		10	20	30	60	90	120	180
<i>B. pyocyaneus</i>	Filter paper.....	+	+	+	-	-	-	-
<i>B. coli communis</i>do.....	+	+	+	-	-	-	-
<i>B. dysenterix</i>do.....	+	+	+	-	-	-	-
<i>B. subtilis</i>do.....	+	+	+	+	+	-	-
<i>B. coli communis</i>	Wilson method.....	+	+	+	-	-	-	-
<i>B. subtilis</i>do.....	+	+	+	+	+	+	+

EXPERIMENT NO. 34.

Generating lamp.

* Methyl alcohol, 1,000 c. c.
Capacity of room, 2,000 cubic feet.
Weather: No wind, cloudy.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before starting lamp.....	64	84	5.51
After 2 hours.....	69	94	7.26
After 3 hours.....	67	92	6.66

Time of exposure of organisms counted from time of starting the lamp.

EXPERIMENT NO. 34—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.			
		30	60	120	180
<i>B. pyocyaneus</i>	Glass.....	—	—	—	—
<i>B. typhosus</i>	do.....	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—
<i>Staphylococcus pyog. aur</i>	do.....	+	—	—	—
<i>B. typhosus</i>	Filter paper.....	—	—	—	—
<i>B. pyocyaneus</i>	Wilson method.....	+	—	—	—

Most of the nonspore-bearing organisms were killed within 1 hour in the above experiments. The spores of *B. subtilis* exposed directly on slips of filter paper were destroyed within 2 hours, while the same organisms exposed by the Wilson method were not killed within 3 hours.

In each experiment the relative humidity was raised almost to saturation at the end of 2 hours; the temperature was also raised several degrees.

The following three experiments (Nos. 35, 36, and 37) were done at a lower temperature than the above experiments. In these the temperature and humidity were raised very materially. Most of the nonspore-bearing organisms were killed within 2 or 3 hours.

In Nos. 36 and 37 the organisms were not exposed until 2 hours after starting the lamp.

EXPERIMENT NO. 35.

Generating lamp.

* Methyl alcohol, 1,000 c. c.
Capacity of room, 2,000 cubic feet.
Weather: Cloudy, light wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before starting lamp.....	42	69	2.11
After 2 hours.....	49	86	3.38
After 4 hours.....	52	84	3.66

Time of exposure of organisms counted from time of starting the lamp.

EXPERIMENT NO. 35—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.				
		30	60	120	180	240
<i>B. typhosus</i>	Filter paper.....	+	+	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+

EXPERIMENT NO. 36.

Generating lamp.

* Methyl alcohol, 1,000 c. c.

Capacity of room, 2,000 cubic feet.

Weather: Moderate, northerly wind; clear.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before starting lamp.....	44	63	2.07
After 2 hours.....	52	94	4.11
After 5 hours.....	51	87	3.68

Organisms exposed 2 hours after starting lamp.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		10	20	30	45	60	120	180
<i>B. typhosus</i>	Filter paper.....	+	+	+	+	—	—	—
<i>B. coli communis</i>	do.....	+	+	+	+	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+

EXPERIMENT NO. 37.

Generating lamp.

* Methyl alcohol, 1,000 c. c.

Capacity of room, 2,000 cubic feet.

Weather: No wind; snowing.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before starting lamp.....	39	59	1.62
After 2 hours.....	45	93	3.17
After 5 hours.....	39	92	2.71

Organisms exposed 2 hours after starting lamp.

EXPERIMENT NO. 37—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.						
		10	20	30	45	60	120	180
<i>B. typhosus</i>	Filter paper.....	+	+	+	+	+	—	—
<i>B. coli communis</i>do.....	+	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+	+
<i>B. coli communis</i>	Wilson method.....	+	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+	+

* For rooms of this size the U. S. Quarantine regulations require 1440 c. c. of methyl alcohol.

With this method, under proper conditions of temperature and humidity, most of the nonspore-bearing organisms were killed within a reasonable time. The time, however, is longer than with the previous methods. Spores usually escaped destruction or were killed only after a relatively long time.

As has been stated, the organisms were usually exposed and the time of exposure counted from the time of starting the lamp. This was not the case with the retort and autoclave methods, which required approximately 1 hour for the former and 25 minutes for the latter to vaporize the formalin. Therefore, in making a comparison of the time required for germicidal efficiency in these three methods the time at which the exposures were made must be borne in mind.

With the lamp the organisms were, of course, subjected to the action of the formaldehyde as it was given off and probably many of them were destroyed before the process of liberation was complete. This fact also is to be considered in comparing the time actually required to kill the organisms in the three methods.

The lamp is the only method that raises the temperature to any appreciable extent. The humidity is also increased considerably, and as it comes principally from evaporation of the water in the lamp, it is very probable that it is more like the natural humidity of the atmosphere, and consequently is more potent in formaldehyde disinfection than is the moisture given off by the other methods.

As has already been stated, the temperature and humidity are of paramount importance in disinfecting with formaldehyde. On the other hand, its employment has the objections that have been mentioned in case of the retort and autoclave, namely, that special apparatus is required and time is consumed in evolving the formaldehyde. An important feature of this lamp generator is that there is no polymerization of formaldehyde into paraform following its use.

VII. FORMALIN-ALUMINUM SULPHATE-LIME METHOD.

This method of liberating formaldehyde gas from formalin was first described by Walker,^a of the department of health, Brooklyn, N. Y.

^a Walker, Henry G.: On a new method of generating formaldehyde gas for fumigating purposes. Journ. Am. Chem. Soc., vol. 24, No. 3, March, 1905.

He dissolves 20 to 25 pounds of commercial aluminum sulphate in 5 gallons of hot water and mixes this solution with 15 gallons of 40 per cent formaldehyde solution. Eight fluid ounces of this mixture and 1 pound of lime are used for 1,000 cubic feet. He recommends that the lime be used in small particles and that it should slake rapidly in cold water. We used the method practically as recommended by Walker.

Aluminum sulphate was added to hot water in the proportion of 50 grams of the former to 100 c. c. of the latter. For an experiment 300 c. c. of this solution, 600 c. c. of formalin, and 2,000 grams of unslaked lime were usually used. Before using the lime it was broken into small particles and placed in a large bucket in the room. When ready to start, the formalin and aluminum sulphate solution were mixed and poured over the lime. The lime began to slake in a few minutes and continued about 20 minutes, during which time considerable formaldehyde, steam, etc., were given off. At the end of this time the process of liberation appeared to be completed.

Chemical determinations were made in the usual way, allowing about 40 minutes to elapse after starting an experiment before beginning to draw air from the room. As it was soon found that the percentage of formaldehyde liberated by this method is relatively low, only a few experiments were done. About 14 per cent was found, which is less than half that liberated by several of the other methods. After the experiment was over (2 hours) the lime was found completely slaked and in a perfectly dry state.

A summary of conditions and results is given in each of the following experiments performed for the purpose of determining the disinfecting value of this method:

EXPERIMENT NO. 38.

Formalin-aluminum sulphate-lime method.

Formalin, 600 c. c.

Solution of aluminum sulphate in water (proportion of 50 grams to 100 c. c. of water), 300 c. c.,
Unslaked lime (in small particles), 2,000 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Quantity of formaldehyde found per cubic foot, 0.01498 gram.

(Determination made by drawing air from room beginning 40 minutes after mixing the formalin-aluminum solution and lime.)

Yield of formaldehyde, 14 per cent.

Weather: Practically no wind; warm and rainy.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing formalin, aluminum sulphate, and lime.....	87	66	8.92
After 10 minutes.....	87.5	85	11.67
After 20 minutes.....	87.5	83	11.39
After 2 hours.....	88.0	81	11.29

Time of exposure of organism counted from time of mixing the formalin-aluminum solution and lime.

EXPERIMENT NO. 38—Continued.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.					
		5	10	20	30	45	60
<i>B. coli communis</i>	Glass.....	+	—	—	—	—	—
<i>B. subtilis</i>	do.....	—	—	—	—	—	—
<i>B. pyocyaneus</i>	Filter paper.....	+	+	—	—	—	—
<i>B. typhosus</i>	do.....	+	+	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	—	—
<i>B. coli communis</i>	Wilson method.....	+	+	—	—	—	—

EXPERIMENT NO. 39.

Formalin-aluminum sulphate-lime method.

Formalin, 600 c. c.

Solution of aluminum sulphate in water (proportion of 50 grams to 100 c. c. of water), 300 c. c.

Water, 300 c. c.

Unslaked lime, 2,500 grams.

Capacity of room, 2,000 cubic foot.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Percentage yield of formaldehyde undetermined.

Weather: Light westerly wind, cloudy.

	Temperature.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing formalin, aluminum sulphate, and lime.....	71	58	4.78
After 10 minutes.....	72	82	6.98
After 20 minutes.....	72	86	7.31
After 3 hours.....	74	65	5.89

Time of exposure of organism counted from time of mixing the formalin-aluminum solution and lime.

[+ means growth; — no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.							
		10	20	30	45	60	90	120	180
<i>B. pyocyaneus</i>	Glass.....	+	+	—	—	—	—	—	—
<i>B. coli communis</i>	do.....	+	—	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	—	—	—
<i>B. typhosus</i>	Filter paper.....	+	—	—	—	—	—	—	—
<i>B. coli communis</i>	do.....	+	+	—	—	—	—	—	—
<i>B. subtilis</i>	do.....	+	+	+	+	+	+	+	+

EXPERIMENT NO. 40.

Formalin-aluminum sulphate-lime method.

Formalin, 600 c. c.

Solution of aluminum sulphate in water (proportion of 50 grams to 100 c. c. of water), 300 c. c.

Unslaked lime (in small particles), 2,000 grams.

Capacity of room, 2,000 cubic feet.

Quantity of formaldehyde used per cubic foot, 0.107 gram.

Yield of formaldehyde undetermined.

Weather: Clear; light wind.

	Tempera- ture.	Relative humidity.	Absolute humidity (grams per cubic foot).
	° F.	Per cent.	
Before mixing formalin, aluminum sulphate, and lime.....	69	47	3.63
After 10 minutes.....	69	67	5.17
After 3 hours.....	70	64	5.10

Time of exposure of organism counted from time of mixing the formalin-aluminum solution and lime.

[+ means growth; —, no growth.]

Organism.	How exposed.	Time of exposure in minutes, and results.							
		10	20	30	45	60	90	120	180
<i>B. pyocyaneus</i>	Glass.....	+	+	+	+	—	—
<i>B. coli communis</i>do.....	+	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+	+	+
<i>B. pyocyaneus</i>	Wilson method.....	+	+	+	+	+	+
<i>B. coli communis</i>	Filter paper.....	+	+	+	+	+	+	+
<i>B. subtilis</i>do.....	+	+	+	+	+	+	+	+

The percentage of formaldehyde found in experiment No. 38 was low; but, as the temperature and humidity were comparatively high, the organisms, including the spores of *B. subtilis*, were destroyed in rather a short time.

In experiment No. 39 the temperature and humidity were not so high as in the previous experiment, and consequently the killing power of the formaldehyde was much diminished. The spores of *B. subtilis* exposed on filter paper were not killed within 3 hours. There is certainly nothing in the results of this experiment to indicate that the addition of 300 c. c. of water was of any advantage for disinfection purposes.

A low humidity affects the germicidal power of the formaldehyde in this method to about the same extent as it does in the other methods. This is shown in experiment No. 40, humidity 47 per cent, in which the only organism killed was *B. pyocyaneus* exposed on glass.

This method has nothing to recommend it especially for disinfection purposes unless it is the amount of moisture given off. This is about the same as with the formalin-permanganate method; but, as has been mentioned above, it is an open question what rôle this form of moisture plays in disinfecting with formaldehyde. The percentage

of formaldehyde liberated by this method is less than half that obtained by the formalin-permanganate method. The latter method is also simpler and more easily conducted than the former. For practical disinfection some of the other methods, notably the formalin-permanganate, are superior to the formalin-aluminum-sulphate-lime method; consequently, further experiments with the latter method seemed unnecessary, although under favorable conditions it may be used with very good results.

EXPERIMENTS IN A LARGE BOTTLE WITH THE FORMALIN-PERMANGANATE METHOD.

As the changes in climatic conditions caused variations in the results of the experiments performed in the room, some experiments were performed in a large bottle, in which certain influences would be either eliminated or more amenable to control.

Furthermore, the special purpose of these experiments precluded the possibility of conducting them in a room of any character. This purpose may be briefly summarized as follows: (1) To determine with the formalin-permanganate method under different conditions the quantity of formaldehyde liberated and also the quantity left in the residue in the generator; (2) to determine the minimum relative humidity and lowest temperature at which formaldehyde disinfection is practicable.

Chemical determinations.—The chemical experiments were carried out in two bottles, one holding a trifle over 24 liters (0.85 cubic foot), the other very nearly 18 liters (0.63 cubic foot). The mouths of the bottles were 2.75 inches wide and were closed with tight-fitting corks, the pores of which were sealed with melted paraffin.

A porcelain crucible holding 24 c. c. was fitted into an excavated flat cork, which was suspended in a stirrup of thin twine.

The formalin was practically 40 per cent by volume, as determined by the Blank and Finkenheimer hydrogen dioxide method. The quantity to be used in an experiment, usually 0.7 c. c., was carefully measured from a slender pipette in which 0.1 c. c. made a volume 1.7 cm. long. The formalin was used undiluted in some experiments and in others a definite quantity of water was added to it before mixing with the permanganate.

I. EXPERIMENTS WITH UNDILUTED FORMALIN AND PERMANGANATE.

Method of procedure for determining the percentage of gas liberated.—About 40 c. c. of approximately decinormal potassium cyanide solution were measured from a burette into the bottle and about 50 c. c. of water added. The liquid was then rolled over the side of the bottle to produce a greater absorbing surface. Then the crucible containing

the formaldehyde was suspended in the mouth of the bottle, the permanganate dropped in from a piece of glazed paper, the whole let down quickly into the bottle by a string, and the cork securely placed.

After a few seconds a vigorous action began, which seemed to be over in about 5 minutes. About 15 minutes, however, were allowed to elapse before the crucible was removed. By repeatedly rolling the cyanide solution over the side of the bottle the formaldehyde was soon absorbed (in about half an hour). After the odor of formaldehyde could not be detected the contents of the bottle were transferred by thorough washing to a 500 c. c. flask containing an excess of decinormal silver nitrate (about 10 c. c.) acidified with nitric acid. The volume was made up to the mark, the flask thoroughly shaken, 250 c. c. of the filtrate titrated with sulphocyanate solution, and calculation made as already described.

Method of procedure for the residue in the crucible.—After the crucible was removed, the contents were thoroughly extracted with water and filtered into a 250 c. c. flask. The volume was made up to the mark and 50 c. c. of this liquid were added to about 15 c. c. of the cyanide solution. After stirring, it was poured into an excess of acidified silver nitrate solution, which was stirred until the precipitate collected into a clot. The clear filtrate from the precipitate was then titrated with sulphocyanate solution for excess of silver.

TABLE 6.—*Results of experiments in glass bottles.*

	Experiment, date, etc.	Size of bot- tle, liters.	For- ma- lin (40 per cent) by vol- ume.	KMn O ₄ .	For- malde- hyde found in bottle.	For- malde- hyde found in resi- due.	Total of formal- dehyde found in bottle and residue.	Remarks.
			c. c.	Gm.	Per ct.	Per ct.	Per ct.	
I	Aug. 15, 1905.....	24	1	0.5	33.03	KMnO ₄ in small needle crystals.
II	Aug. 16, 1905.....	24	1	0.5	33.52	38.25	71.77	Do.
III	Aug. 18, 1905.....	18	1	0.5	32.47	40.35	72.82	Do.
IV	Aug. 17, 1905.....	18	0.7	0.35	35.48	33.86	69.34	KMnO ₄ ground to moderately fine powder.
V	Aug. 18, 1905.....	18	0.7	0.35	36.53	35.20	71.73	Do.
VIdo.....	24	1	0.5	35.11	Do.
VII	Aug. 21, 1905.....	18	0.7	0.35	37	32.20	69.20	Do.
VIII	Aug. 22, 1905.....	18	0.7	0.35	37.83	32.76	70.59	Do.
IX	Aug. 19, 1905.....	18	0.5	0.25	33.28	38.10	71.38	Do.
X	Aug. 25, 1905.....	18	0.7	0.4	34.37	25.16	59.53	Do.
XI	Aug. 28, 1905.....	18	1	0.39	25.20	42.79	67.99	Do.
XII	Jan. 3, 1906, 41° F.	18	0.7	0.35	30.84	39.09	69.93	Do.
XIII	Jan. 5, 1906, 41° F.	18	0.7	0.35	30	34.1	64.1	Do.
XIV	Feb. 8, 1906, 34° F.	18	0.7	0.35	30.1	34.15	64.16	Do.
XV	Feb. 3, 1906, 20° F.	18	0.7	0.35	28.26	Do.

Experiments I to XI, inclusive, Table 6, were done during warm weather (summer), and in all but X and XI the proportions used were 1 part by volume of formalin to 0.5 part by weight of permanganate, the same as was used in the experiments in Table 1. With this proportion the total amount of formaldehyde found in the air of the bottle and in the residue was fairly constant, considering the conditions of the experiments.

Evidently there is an advantage in using permanganate in powdered form, as is shown by comparing the results of IV, V, VI, VII, and VIII, with those of I, II, and III. No doubt the reason for this is that action takes place more quickly with production of a higher temperature, so that more formalin evaporates from the crucible and less remains with the residue.

The results in experiments I, II, and III, with an average of 33 per cent, are lower than the results in Table 1, which refer to experiments in charging the room of 2,000 cubic feet. This would be expected considering the small quantities used, whereby the quantity of heat produced is not so large and the cooling of the generator is more rapid. In the experiments where powdered permanganate was used, the percentage yield is higher and in line with the results in Table 1.

In experiment IX, where only 0.5 c. c. of formalin was used, the result is low; but this is probably due to the fact that the quantity of formalin is too small to produce as vigorous an action as did the other cases.

In experiment X the proportion of permanganate was increased, with the result that the amount of the formaldehyde sent out into the bottle was not affected much, but considerably less remained with the residue.

In experiment XI the permanganate was decreased to the proportion used by Evans (Maine State board of health) in the report on this method. The result shows a considerable decrease in the formaldehyde sent out into the bottle and large increase in the amount remaining in the residue.

Experiments XII to XV inclusive were performed during cold weather (winter), the results of which demonstrate that the percentage of formaldehyde actually given off during cold weather does not differ very materially from that given off during warm weather.

In these experiments any paraformaldehyde, whether given off as such or resulting from polymerization of the formaldehyde after it was given off, is included in the percentage of formaldehyde liberated, since paraformaldehyde enters into union with the cyanide in the same manner as does formaldehyde gas.

The results of these experiments also show that the reduced yield of formaldehyde obtained in the room when working at a cold tempera-

ture was not due so much to the cold causing a reduction in the quantity of formaldehyde given off as to polymerization of the liberated formaldehyde resulting from the cold.

II. EXPERIMENT WITH DILUTED FORMALIN AND PERMANGANATE.

Two experiments were made with 0.6 c. c. formalin diluted with 0.3 c. c. water and 0.375 gm. of powdered permanganate; these are the same proportions as used in most of the experiments in Table 2. The procedure was the same as described above.

Experiment.	Formaldehyde found in bottle.	Formaldehyde found in residue.	Total found.
	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>
I.	31.00	34.23	65.23
II.	32.16	34.04	66.20

The percentage yield was about the same as that given in Table 2, but less than that in the previous experiments (Table 6) with undiluted formalin. The formaldehyde remaining with the residue was about the same as in the previous experiments where powdered permanganate was used. The total formaldehyde found was less than in the experiments with undiluted formalin, thus indicating a greater destruction of formaldehyde.

III. EXPERIMENTS ON DRYING FORMALDEHYDE GAS BY ANHYDROUS CALCIUM CHLORIDE.

The bottle was charged as in the previous cases, using 0.7 c. c. of formalin and 0.35 gm. of powdered permanganate. The crucible was removed between 15 and 20 minutes after it had been introduced into the bottle.

The drying apparatus consisted of a curved tray, made of a piece of sheet zinc about 1.75 inches wide, 10 inches long, and 1.25 inches deep. One end of the tray was closed by bringing the edges together; the other end was curved around a wooden handle, which fitted into a hole in a cork. The latter fitted the mouth of the bottle.

After removing the crucible the bottle was laid on its side. Granulated calcium chloride was placed in the tray in a layer about an inch deep; then as quickly as possible the stopper of the bottle was removed and the tray introduced and held in place by means of the stopper attached to its handle, which fitted the neck of the bottle.

After 1 hour, which seemed ample time to thoroughly dry the atmosphere in the bottle because of the large surface of calcium chloride exposed, the stopper and tray were removed and replaced by the first one.

Before introducing the calcium chloride the inner surface of the bottle was covered with moisture. This disappeared in about 15 or 20 minutes after the drying apparatus was introduced.

Naturally a little formaldehyde was lost by displacement and diffusion when the drying tray was introduced and withdrawn. This loss could not have been more than a small fraction of the amount of formaldehyde in the bottle when the crucible was removed.

After withdrawing the drying apparatus, potassium cyanide solution was measured into the bottle from a burette through an inch hole in the stopper. To prevent loss, the burette tip was passed through a small hole in a flat cork, which in turn fitted into the hole of the stopper, thus closing the mouth of the bottle. After removing the burette, the hole in the stopper was properly closed with a cork. The subsequent procedure was exactly like that described above (p. 66).

The formaldehyde left in the residue in the crucible was also determined in the manner already described (p. 67).

TABLE 7.—*Experiments on drying formaldehyde gas in 18-liter bottle by calcium chloride.*

Experiment.	Formalin 40 per cent by volume.	KMnO ₄ pow- dered.	Time of dry- ing.	Formal- dehyde found in bottle.	Formal- dehyde found in residue.
	<i>c. c.</i>	<i>gm.</i>		<i>Per cent.</i>	<i>Per cent.</i>
I.....	0.7	0.35	1 hour.....	21.12	33.86
II.....	.7	.35	½ hour.....	20.06	32.52
III.....	.7	.35	2 hours....	14.76	35.87

Since the bottle was charged in precisely the same manner and with the same quantities as in experiments IV, V, VII, and VIII, Table 6, we may assume that the average of these four results, namely, 36.71 per cent is the quantity of formaldehyde in the bottle in the present experiments before drying. The results of experiments I and II, Table 7, are fairly close, the average being 20.59 per cent. The difference, 16.12 per cent is the loss, due mainly to drying and, in a small degree, to escape by introduction and removal of the drying apparatus. It is probable that more than one-third of the formaldehyde disappeared by the drying during 1 hour. By 2 hours' drying still more disappeared, as shown in experiment III.

The question as to what becomes of the formaldehyde that disappears is an interesting one; but it was not investigated. After the calcium chloride had been removed from the bottle it was stored in a closed jar. This jar had a strong odor of the gas. It is probable that some of the formaldehyde was held as such in the pores of the calcium chloride granules. Whether the latter also had a polymerizing effect on the formaldehyde we are not able to say.

The quantities of formaldehyde found remaining with the residue in the porcelain crucible (average 34.08 per cent) agree fairly well with the results in experiments IV, V, VII, and VIII, Table 6 (average 33.50 per cent).

IV. HUMIDITY AND TEMPERATURE IN FORMALDEHYDE DISINFECTION.

The influence and importance of humidity and temperature became very evident in many of the experiments, but owing to uncontrollable circumstances in the room their minimum limitations, particularly of the humidity, could not be closely approximated. It will readily be seen that it is of more practical importance to know this in case of the humidity than of the temperature, since the former is subject to wide variations even within a few hours. For instance, the humidity of the atmosphere may be 90 per cent at 8 a. m., 30 per cent at 2 p. m., and 90 per cent again at 8 p. m. of the same day. Such variations in temperature seldom, if ever, occur in so short a time. As we had observed in the room experiments that formaldehyde is inefficient as a disinfectant when employed during cold weather, most of the experiments for determining the minimum limitations of humidity were done at ordinary summer temperatures. For conducting the experiments a large bottle holding 24 liters (0.85 cubic foot) was used. As this bottle, the mode of setting off the formalin and permanganate, the process of drying with calcium chloride, etc., have already been fully described (p. 66), only the more important details will be given here.

The quantities of formalin and permanganate used were in the proportion of 1 c. c. of the former to 0.5 gram of the latter. The formalin contained about 40 per cent of formaldehyde by volume. The result of mixing the formalin and permanganate in the above proportions was a vigorous reaction, which, in addition to evolving formaldehyde, gave off rather a large quantity of aqueous vapor, which settled on the sides of the bottle to such an extent as to make the glass almost non-transparent.

A few experiments easily demonstrated that with a high temperature, say 80° F., even a small percentage of formaldehyde with a large quantity of moisture, is a most powerful surface disinfectant, killing 40-day old spores of *Bacillus subtilis* in a few minutes.

The object then was to remove the moisture in the bottle by introducing a metal tray containing anhydrous calcium chloride, after which a definite quantity of water could be injected in the form of aqueous vapor.

Soon after introducing the calcium chloride the moisture from the sides of the bottle would disappear. The atmosphere in the bottle was assumed to be in a dry condition after about 1 hour, and the tray

containing the calcium chloride was then removed. A thermometer was then introduced and the temperature in the bottle determined. Having ascertained this, the quantity of water necessary to give a certain percentage of relative humidity was easily estimated by referring to the psychrometric tables for obtaining the vapor pressure, relative humidity, and temperature of the dew-point, prepared by the weather Bureau, United States Department of Agriculture.

The desired quantity of water was measured in a graduated pipette and placed in a test tube, the open end of which had been drawn out into a small tube about 0.5 centimeter in diameter; to be more accurate, the tube with its contents was then carefully weighed. The small end of the test tube was introduced into the bottle and the other end gently heated. This caused the water to pass into the bottle in the form of steam. After vaporizing the water, the tube was left in place until it had cooled; this caused some of the moisture to recondense on the sides of the tube. The tube was removed and again carefully weighed, the difference in the two weighings giving the quantity of water actually injected in the form of aqueous vapor.

This factor, and the temperature, being known, the percentage of relative humidity was easily computed from the tables referred to above (p. 72). The exact degree of relative humidity desired was often not easily obtained, as it was difficult to inject the precise quantity of water wanted, and, furthermore, the temperature was subject to change. The slightest variation in either 1 of these 2 factors gives a different percentage of relative humidity.

For making the bacteriological exposures, 24-hour old agar cultures of *B. coli communis* and spores of *B. subtilis*, grown about 40 days on agar slants, were used. An emulsion of the organisms in distilled water was made, small slips of filter paper about 0.5 cm. square were moistened with the emulsion and placed in the incubating room for about 1 hour in order to thoroughly dry them.

The slips of filter paper were then placed in a small copper-wire tray, previously sterilized, and exposed to the action of the formaldehyde in the bottle by introducing through a hole in the large cork stopper. This tray was provided with a tight-fitting cork on the near end, so that when the tray was in place in the bottle the cork would close the hole through which it was introduced. This arrangement made it possible to withdraw the tray wholly or partly when desired. The slips of filter paper were taken out at definite intervals and planted in tubes of nutrient bouillon. The tubes were then placed in the incubating room at a temperature of 37° C. and the results recorded after 10 days' incubation.

TABLE 10.

Experiments in a 24-liter bottle.
 Formalin-permanganate method.
 Formalin 0.5 c. c. and permanganate 0.25 gram.
 Moisture removed by calcium chloride.
 Varying quantities of moisture introduced.
 Ordinary summer temperatures.
B. coli communis exposed on filter paper.

[+ means growth; — no growth.]

Temperature at time of experiment.	Quantity of water injected as aqueous vapor.		Time of exposure in minutes, and results.									
	Absolute humidity, grains per cubic foot.	Relative humidity.										
			5	10	15	20	30	45	60	75	90	120
77.0	6.17	62	+	+	—	—	—	—	—	—	—	—
77.5	5.44	54	+	+	+	+	—	—	—	—	—	—
75.0	4.64	50	+	+	+	+	+	+	+	+	+	+

TABLE 11.

Experiments in a 24-liter bottle.
 Formalin-permanganate method.
 Formalin 0.5 c. c. and permanganate 0.25 gram.
 Moisture removed by calcium chloride.
 Varying quantities of moisture introduced.
 Ordinary summer temperatures.
B. subtilis exposed on filter paper.

[+ means growth; — no growth.]

Temperature at time of experiment.	Quantity of water injected as aqueous vapor.		Time of exposure in minutes, and results.									
	Absolute humidity, grains per cubic foot.	Relative humidity.										
			5	10	15	20	30	45	60	75	90	120
77.0	6.17	62	+	+	+	+	+	—	—	—	—	—
77.5	5.44	54	+	+	+	+	+	+	—	—	—	—
75.0	4.64	50	+	+	+	+	+	+	+	+	+	+

It will be observed from the above experiments that with a relative humidity between 50 and 60 per cent both *B. coli communis* and *B. subtilis* were killed within a reasonably short time, but below 50 per cent neither organism was killed within 2 hours.

These results demonstrate the important part that humidity plays in formaldehyde disinfection and that the minimum limit lies between 50 and 60 per cent. This is a slightly smaller percentage than was found necessary in the room experiments to accomplish disinfection; but of course the conditions in the bottle were unusually favorable for germicidal action and slightly better results would therefore be expected.

The different temperatures at which the experiments were performed may account for some of the little variations in the results of the above tables (8-11).

The question might arise whether absolutely all of the moisture was removed from the bottle by the calcium chloride after 1 hour exposure; but from the known chemical affinity of this substance for water it would seem that all of it was absorbed.

If all the moisture was removed from the bottle by the calcium chloride, the idea that once prevailed, namely, that formaldehyde can not exist in a perfectly dry state, is disproved.

A comparison of the percentage of humidity required in these experiments with that required in the room experiments (p. 29), would seem to indicate that the moisture given off by the process of liberation in the latter experiments is of much less importance than the moisture in the air before the experiment is started.

It is not so much the absolute as the relative humidity that is necessary in formaldehyde disinfection. For example, the action of an ordinary quantity of formaldehyde is strongly germicidal in the presence of 5.586 grains (0.36 gram) of moisture per cubic foot at a temperature of 70° F. (relative humidity 70 per cent), but is almost inert in the presence of 6.85 grains (0.443 gram) per cubic foot at a temperature of 95° F. (relative humidity 40 per cent).

By referring to Table 7 it will be seen that a large quantity of formaldehyde was removed from the bottle in the process of drying. It may be assumed from our experimental determinations that before drying, the bottle contained 36.71 per cent of the formaldehyde theoretically present in the quantity of formalin used. By drying 1 hour with calcium chloride the quantity of formaldehyde was reduced to about 20.5 per cent and after 2 hours to 14.76 per cent.

To show the germicidal power of a reduced quantity of formaldehyde in the presence of a high humidity and temperature two experiments were done, using one-fourth the original quantities of formalin and permanganate used in Tables 8 and 9, namely, formalin 0.25 c. c. and permanganate 0.125 gram.

In one experiment with a relative humidity of 61 per cent, temperature 26° F., *B. coli communis* was killed within 30 minutes. In the other, with relative humidity of 59 per cent, temperature 60° F., the same species was killed within the same time. *B. subtilis*, exposed in both experiments at the same time as *B. coli communis*, were not killed within 2 hours.

Two more experiments were performed in which one-eighth the original quantities of formalin and permanganate were used, namely, formalin 0.125 c. c. and permanganate 0.0625 gram. In one, with a relative humidity of 75 per cent, temperature 74° F., *B. coli communis* was killed within 30 minutes, while in the other, with a relative humidity of 59 per cent, temperature 70° F., the same species was killed within one hour. *B. subtilis*, exposed at the same time as *B. coli communis*, was not killed in either experiment within 2 hours.

Comparison of Tables 8, 9, and 12 shows that the time required for germicidal action is materially increased by a reduction in temperature, even though it is not below 60° F.

This is more noticeable with *B. subtilis* than with *B. coli communis*. At a lower temperature the killing power of the formaldehyde becomes so limited that only a few experiments were performed at a temperature lower than 60° F. With a temperature of 40° F. and humidity of 95 per cent, *B. coli communis* was killed within an hour and a half; but, considering the method of exposing, the organism, and the fact that as high humidity as that is rarely observed at that temperature except under artificial conditions the results can not be considered satisfactory.

DISINFECTION OF SLEEPING CARS WITH FORMALDEHYDE GAS.

These experiments were conducted for the purpose of determining the practical value and efficiency of the formalin-permanganate method of liberating formaldehyde gas in the disinfection of sleeping cars.

For comparison, experiments were also done with other well-known methods of evolving the gas for disinfection purposes. The work was done in the cars of the Pullman Company at their local yards. We are indebted to the officials of this company for the use of the cars and their cooperation and assistance in carrying out this work. The cars were selected at random, regardless of when they had been occupied; usually they had been used the previous night. Often the cars were shifted about in the yard during the experiment. Although the size of the different cars varied slightly, for our purposes their air space was approximately 4,500 cubic feet.

Usually 2,000 c. c. of formalin, containing 35.66 per cent by volume of formaldehyde, were used for an experiment. Before starting all berths were let down, inside doors opened, and windows and ventilators closed. When practicable, the lamp ventilators were closed on the inside with cotton waste; otherwise they were closed on top of the car by wrapping cloths around them. No pasting of cracks was done.

All organisms used, except *B. tuberculosis*, were grown, prepared, and exposed by the Wilson method, as described on page 17. For *B. tuberculosis*, tuberculous sputum, showing on examination many tubercule bacilli, was used. Exposures of this were made by the Wilson method and on small pieces of carpet, using in each case a drop or two of the sputum. For convenience and safety, the pieces of carpet were carried in a Petri dish and exposed in the car by simply removing the top of the dish. After preparing the exposures they were dried in the incubator at a temperature of 37° C. for 1 hour, and, as the laboratory is some distance from the car yards, about another hour

elapsed before the exposures were made. They were variously placed in the car for exposure, the exact location being recorded in each case.

Different lengths of exposure might have been tried, but in our experiments 2 hours was chosen. Therefore, the car in all experiments was opened after 2 hours from the time of beginning to liberate the gas. The organisms were removed from the car as soon thereafter as possible, usually about 15 minutes, and taken to the laboratory. With the exception of *B. tuberculosis*, they were planted in nutrient bouillon, placed in the incubating room, and the results recorded; as has been described (p. 18).

In case of *B. tuberculosis*, the pieces of carpet and slips of filter paper (Wilson method) were washed in bouillon and the washings injected intraperitoneally into guinea pigs. Control pigs were also inoculated at the same time. The pigs were weighed before and at definite intervals after inoculation; those that did not die within about 3 months were chloroformed. A careful post-mortem examination was made of all. The gain or loss of the chloroformed pigs is given in each experiment; the figures refer to the weight of the pig when inoculated as compared with its weight when chloroformed.

Although the cars seemed comparatively tight, the small percentage of formaldehyde gas found in the cars on opening showed that much of it had escaped during the 2 hours. The temperature and relative humidity were taken just before starting an experiment and again as soon after it was over as possible. The second reading, however, indicates more the condition of the outside atmosphere than any change resulting from the experiment, as the car was then being aired.

I. FORMALIN-PERMANGANATE METHOD.

Formalin and permanganate were used in these experiments in the same proportions as given on page 20, namely, 1 c. c. of the former to 0.5 gram of the latter. The ordinary commercial crystals of permanganate were used without further powdering. The formalin and permanganate were mixed in galvanized-iron buckets, one being used for every 500 c. c. of formalin, and placed in the car as described in each experiment. As the quantities of the formalin and permanganate used, the condition of the weather, including temperature, relative humidity, winds, etc., are given in each individual experiment, further description here is unnecessary. The experiments are as follows:

EXPERIMENT No. 41.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear; light southerly wind.

Temperature in car at beginning of experiment, 83° F.

Relative humidity in car at beginning of experiment, 78 per cent.

Time of exposure, 2 hours (11.15 a. m. to 1.15 p. m.).

Temperature in car after opening and airing 15 minutes, 87° F.

Relative humidity in car after opening and airing 15 minutes, 62 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, lower No. 6	—
<i>B. diphtheriæ</i>	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, upper No. 4	—
	Berth, lower No. 8	—
<i>B. typhosus</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, upper No. 6	—
<i>B. subtilis</i>	Smoking room	—
	Drawing-room	—
	Berth, upper No. 10	—
	Berth, lower No. 8	—
<i>B. tuberculosis</i>	Smoking room	—
	Sputum exposed and injected into guinea pig; pig chloroformed 100th day; increased 255 grams in weight; no lesions of tuberculosis.	
	Floor of main sleeping compartment	—
	Sputum exposed and injected into guinea pig; pig chloroformed 100th day; increased 235 grams in weight; no lesion of tuberculosis. Control pig died of tuberculosis 45th day.	

EXPERIMENT NO. 42.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear; very light breeze; light rain previous night.

Temperature in car at beginning of experiment, 80° F.

Relative humidity in car at beginning of experiment, 81 per cent.

Time of exposure, 2 hours (11.20 a. m. to 1.20 p. m.).

Temperature in car after opening and airing 15 minutes, 83° F.

Relative humidity in car after opening and airing 15 minutes, 72 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	—
	Smoking room	—
	Drawing-room	+
	Floor main sleeping compartment	—
	Berth, upper No. 2	—
<i>B. diphtheriæ</i>	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, upper No. 10	—
<i>B. yphosus</i>	Berth, lower No. 4	—
	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
<i>B. subtilis</i>	Berth, lower No. 9	—
	Smoking room	—
	Toilet room	—
<i>B. tuberculosis</i>	Drawing-room	—
	Berth, upper No. 4	+
	Smoking room	—
	Sputum exposed and injected into guinea pig; pig chloroformed 103d day; increased 225 grams in weight; no lesions of tuberculosis.	
	Floor of main sleeping compartment	—
	Sputum exposed and injected into guinea pig; pig chloroformed 103d day; increased 260 grams in weight; no lesion of tuberculosis.	
	Control pig died of tuberculosis 45th day.	

EXPERIMENT NO. 43.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear and dry, with practically no wind.

Temperature in car at beginning of experiment, 77.5° F.

Relative humidity in car at beginning of experiment, 69 per cent.

Time of exposure, 2 hours (11.45 a. m. to 1.45 p. m.).

Temperature in car after opening and airing 15 minutes, 83° F.

Relative humidity in car after opening and airing 15 minutes, 53 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Berth, upper No. 9	—
	Berth, lower No. 8	—
<i>B. diphtheriæ</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, lower No. 6	—
<i>B. pyocyaneus</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
<i>B. subtilis</i>	Toilet room	—
	Smoking room	—
	Drawing-room	+
	Berth, lower No. 2	+

EXPERIMENT NO. 44.

Formalin, 2,000 c. c.; permanganate, 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alley way at each end.

Weather: Very cloudy and few drops of rain falling at times; no wind.

Temperature in car at beginning of experiment, 75° F.

Relative humidity in car at beginning of experiment, 82 per cent.

Time of exposure, 2 hours (12 m. to 2 p. m.) .

Temperature in car after opening and airing 20 minutes, 81° F.

Relative humidity in car after opening and airing 20 minutes, 72 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Berth, upper No. 2.....	—
	Berth, lower No. 5.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Drawing-room.....	—
	Berth, upper No. 6.....	—
	Berth, lower No. 1.....	—
<i>B. pyocyaneus</i>	Berth, lower No. 12.....	—
	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Berth, upper No. 2.....	—
<i>Staphylococcus pyogenes aureus</i> .	Berth, lower No. 5.....	—
	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor, main sleeping compartment.....	—
	Berth, upper No. 1.....	—
	Berth, lower No. 6.....	—
<i>B. subtilis</i>	Smoking room.....	+
	Drawing-room.....	+
	Berth, upper No. 2.....	+
	Berth, lower No. 12.....	+

EXPERIMENT NO. 45.

Formalin, 2,000 c. c.; permanganate, 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alley way at each end.

Weather: Clear and dry, with light variable wind.

Temperature in car at beginning of experiment, 74° F.

Relative humidity in car at beginning of experiment, 65 per cent.

Time of exposure, 2 hours (11.30 a. m. to 1. 30 p. m.).

Temperature in car after opening and airing 15 minutes, 82° F.

Relative humidity in car after opening and airing 15 minutes, 58 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor, main sleeping compartment.....	+
	Berth, lower No. 10.....	—
<i>B. diphtheriæ</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor, main sleeping compartment.....	—
	Berth, upper No. 8.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Berth, upper No. 4.....	—
	Berth, upper No. 10.....	—
<i>B. subtilis</i>	Smoking room.....	—
	Toilet room.....	—
	Drawing-room.....	+
	Berth, upper No. 8.....	—
	Berth, upper No. 4.....	+
<i>B. tuberculosis</i>	Smoking room.....	—
	Sputum exposed and injected into guinea pig. Pig chloroformed 105th day; increased 325 grams in weight; no lesions of tuberculosis.	
	Floor of main sleeping compartment.....	—
	Sputum exposed and injected into guinea pig; pig chloroformed 105th day; increased 245 grams in weight; no lesion of tuberculosis.	
	Drawing-room.....	—
	Sputum exposed and injected into guinea pig; pig chloroformed 105th day; increased 270 grams in weight; no lesions of tuberculosis.	
	Control guinea pig died of tuberculosis 45th day.	

EXPERIMENT NO. 46.

Formalin, 2,000 c. c.; permanganate, 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment and one in the alley-way at each end.

Weather: Clear, practically no wind.

Temperature in car at beginning of experiment, 73° F.

Relative humidity in car at beginning of experiment, 61 per cent.

Time of exposure, 2 hours (11.45 a. m. to 1.45 p. m.).

Temperature in car after opening and airing 15 minutes, 83° F.

Relative humidity in car after opening and airing 15 minutes, 45 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Drawing-room.....	—
	Floor, main sleeping compartment.....	—
	Berth, upper No. 8.....	—
	Berth, lower No. 9.....	—
<i>B. diphtheriæ</i>	Toilet room.....	—
	Drawing-room.....	—
	Floor, main sleeping compartment.....	—
	Berth, lower No. 12.....	—
	Berth, upper No. 8.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Drawing-room.....	—
	Floor, main sleeping compartment.....	—
	Berth, lower No. 6.....	—
	Berth, upper No. 10.....	—
<i>B. subtilis</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 4.....	+
	Berth, lower No. 4.....	+
<i>B. tuberculosis</i>	Floor, main sleeping compartment.....	+
	Sputum exposed by Wilson method and injected into guinea pig; pig chloroformed 25th day; increased 250 grams in weight; lesions of tuberculosis in spleen and lymph glands.	
	Floor, main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 95th day; lesions of tuberculosis in spleen and lungs. Control guinea pig died of tuberculosis 60th day.	

Under ordinary conditions in disinfecting sleeping cars the formalin-permanganate method practically accomplishes complete surface disinfection when the weather is warm and the relative humidity high. The exact temperature and percentage of relative humidity necessary can not be stated within a few degrees, but it will be seen from the experiments that when the temperature is above 74° F. and the relative humidity above 61 per cent nearly all the nonspore-bearing organisms exposed to the action of the gas were killed within 2 hours.

Frequently old *subtilis* spores were killed in the short exposure of 2 hours, as will be seen in the experiments. Most of the tubercle bacilli exposed to the action of the gas were also killed in this time. In a few instances tubercle bacilli were not killed, but they were diminished in virulence. It is probable that a longer exposure than 2 hours would be more effective in this regard.

In the following experiments (Nos. 47 to 54, inclusive) it will be seen that when the temperature is relatively cold or the humidity comparatively low the formaldehyde gas fails to kill many of the organisms exposed.

It is especially interesting to note in the following experiments that while the results can not be considered satisfactory from a practical standpoint, because many of the organisms exposed escaped destruction, nevertheless the interesting point is brought out that organisms exposed in the toilet room of the sleeping car were almost invariably killed. No doubt the reason for this is the greater amount of moisture in the toilet room owing to the water present. As the toilet room is probably more apt to be infected than any other part of the coach, this is a matter of considerable practical value.

EXPERIMENT NO. 47.

Formalin 1,500 c. c., permanganate 750 grams, equally distributed in three iron buckets, one of which was placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, light variable wind.

Temperature in car at beginning of experiment, 78° F.

Relative humidity in car at beginning of experiment 63 per cent.

Time of exposure, 2 hours (12 m. to 2 p. m.).

Temperature in car after opening and airing 15 minutes, 83° F.

Relative humidity in car after opening and airing 15 minutes, 58 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Berth, upper No. 3.....	—
	Berth, lower No. 6.....	+
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 12.....	—
	Berth, lower No. 11.....	—
<i>B. pyocyaneus</i>	Berth, lower No. 3.....	—
	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	+
	Berth, upper No. 3.....	+
	Berth, upper No. 8.....	—
<i>Staphylococcus pyogenes aureus</i>	Berth, lower No. 4.....	—
	Berth, lower No. 11.....	—
	Toilet room.....	—
	Smoking room.....	—
	Berth, upper No. 6.....	+
<i>B. subtilis</i>	Berth, upper No. 12.....	+
	Berth, lower No. 3.....	—
	Smoking room.....	+
	Berth, upper No. 11.....	+
	Berth, lower No. 3.....	+

It is worthy of note here that although only half the quantities of formalin and permanganate were used in the preceding experiment as in the following one, the germicidal results in the former were better than in the latter. As the temperature was practically the same in the two experiments the difference in results is no doubt due to the higher humidity in the former experiment. This shows the importance of humidity in disinfecting with formaldehyde gas, and, further, that regardless of the quantity of gas present the humidity should not be below a certain percentage.

EXPERIMENT NO. 48.

Formalin 3,000 c. c., permanganate 1,500 grams, equally distributed in six iron buckets, four of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear and dry, light wind.

Temperature in car at beginning of experiment, 77.5° F.

Relative humidity in car at beginning of experiment, 58 per cent.

Time of exposure, 2 hours (11.20 a. m. to 1.20 p. m.).

Temperature in car after opening and airing 20 minutes, 83° F.

Relative humidity in car after opening and airing 20 minutes, 48 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Drawing-room.....	+
	Floor main sleeping compartment.....	—
	Berth, upper No. 10.....	+
	Berth, lower No. 6.....	—
<i>B. diphtheriæ</i>	Drawing-room.....	—
	Berth, upper No. 6.....	—
	Berth, lower No. 10.....	+
<i>B. typhosus</i>	Toilet room.....	—
	Drawing-room.....	+
	Berth, upper No. 2.....	—
	Berth, lower No. 2.....	—
	Berth, lower No. 4.....	+
<i>B. subtilis</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 2.....	+
	Berth, lower No. 4.....	+
<i>B. tuberculosis</i>	Floor main sleeping compartment.....	+
	Sputum exposed by the Wilson method and injected into guinea pig; pig chloroformed 92d day; increased 415 grams in weight; spleen had only slight appearance of tuberculosis.	
	Floor main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig died of tuberculosis on 90th day. Control guinea pig died of tuberculosis 63d day.	

EXPERIMENT NO. 49.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, light southerly wind.

Temperature in car at beginning of experiment, 75.5° F.

Relative humidity in car at beginning of experiment, 56 per cent.

Time of exposure, 2 hours (1.10 p. m. to 3.10 p. m.).

Temperature in car after opening and airing 15 minutes, 77.5° F.

Relative humidity in car after opening and airing 15 minutes, 47 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Drawing-room.....	—
	Smoking room.....	+
	Berth, upper No. 8.....	—
	Berth, lower No. 4.....	+
<i>B. diphtheriæ</i>	Toilet room.....	—
	Drawing-room.....	—
	Smoking room.....	+
	Berth, upper No. 9.....	+
	Berth, lower No. 4.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Berth, upper No. 9.....	—
	Berth, lower No. 4.....	+
<i>B. subtilis</i>	Toilet room.....	+
	Smoking room.....	+
	Drawing-room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 10.....	+

EXPERIMENT NO. 50.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, rather strong southerly wind.

Temperature in car at beginning of experiment, 78° F.

Relative humidity in car at beginning of experiment, 53 per cent.

Time of exposure, 2 hours (12.30 p. m. to 2.30 p. m.).

Temperature in car after opening and airing 15 minutes, 79° F.

Relative humidity in car after opening and airing 15 minutes, 50 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	+
	Drawing-room.....	+
	Berth, upper No. 9.....	+
	Berth, lower No. 6.....	+
<i>B. pyocyaneus</i>	Toilet room.....	—
	Drawing-room.....	+
	Smoking room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 1.....	—
	Berth, upper No. 4.....	+
	Berth, upper No. 9.....	+
	Berth, lower No. 7.....	+
	Berth, lower No. 12.....	+
	Toilet room.....	—
<i>B. typhosus</i>	do.....	—
	Smoking room.....	—
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 5.....	—
	Berth, upper No. 6.....	+
	Berth, lower No. 1.....	—
	Berth, lower No 11.....	—
	Toilet room.....	—
	Smoking room.....	+
<i>Staph. pyog. aur</i>	Drawing-room.....	+
	Berth, upper No. 9.....	+
	Berth, lower No. 6.....	+
	Berth, upper No. 1.....	+
<i>B. tuberculosis</i>	Sputum exposed and injected into guinea pig; pig chloroformed 75th day; lost 25 grams in weight; marked lesions of tuberculosis.	
	Berth, lower No. 12.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 75th day; lost 30 grams in weight; marked lesions of tuberculosis.	
	No control pig inoculated.	

EXPERIMENT NO. 51.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear moderate westerly wind.

Temperature in car at beginning of experiment, 71° F.

Relative humidity in car at beginning of experiment, 48 per cent.

Time of exposure, 2 hours (12 m. to 2 p. m.).

Temperature in car after opening and airing 15 minutes, 74° F.

Relative humidity in car after opening and airing 15 minutes, 58 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	+
	Smoking room	+
	Drawing room	+
	Berth, upper No. 2	+
	Berth, lower No. 7	+
<i>B. pyocyaneus</i>	Toilet room	+
do	+
	Smoking room	+
	Floor main sleeping compartment	+
	Berth, upper No. 2	+
	Berth, upper No. 11	+
	Berth, lower No. 5	+
<i>B. typhosus</i>	Toilet room	—
do	—
	Smoking room	—
	Drawing room	+
	Floor main sleeping compartment	+
	Berth, upper No. 11	—
	Berth, lower No. 12	+
<i>Staph. pyog. aur</i>	Toilet room	+
	Smoking room	+
	Floor main sleeping compartment	+
	Berth, upper No. 1	+
	Berth, lower No. 6	+
<i>B. tuberculosis</i>	Floor main sleeping compartment	+
	Sputum exposed and injected into guinea pig; pig chloroformed 77th day; increased 50 grams in weight; marked lesions of tuberculosis.	
	Berth, upper No. 10	+
	Sputum exposed and injected into guinea pig; pig chloroformed 77th day; increased 80 grams in weight; marked lesions of tuberculosis.	
	No control pig inoculated.	

EXPERIMENT NO. 52.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, rather strong northerly wind.

Temperature in car at beginning of experiment, 70° F.

Relative humidity in car at beginning of experiment, 48 per cent.

Time of exposure, 2 hours (11.25 a. m. to 1.25 p. m.).

Temperature in car after opening and airing 15 minutes, 72° F.

Relative humidity in car after opening and airing 15 minutes, 45 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	+
	Berth, upper No. 10.....	—
	Berth, lower No. 9.....	+
<i>B. diphtheriz</i>	Toilet room.....	—
	Smoking room.....	+
	Drawing room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 8.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	+
	Berth, upper No. 4.....	—
	Berth, lower No. 10.....	+
<i>B. subtilis</i>	Smoking room.....	+
	Drawing room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 2.....	+
	Berth, lower No. 6.....	+
<i>B. tuberculosis</i>	Floor of main sleeping compartment.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 87th day; increased 125 grams in weight; tuberculous lesions in liver, spleen, lymph glands, etc.	
	Floor of main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 87th day; increased 40 grams in weight; marked tuberculous lesions in liver, spleen, glands, etc.	
	Control guinea pig died of tuberculosis 50th day.	

EXPERIMENT NO. 53.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, practically no wind.

Temperature in car at beginning of experiment, 65° F.

Relative humidity in car at beginning of experiment, 44 per cent.

Time of exposure, 2 hours (8.25 a. m. to 10.25 a. m.).

Temperature in car after opening and airing 15 minutes, 69° F.

Relative humidity in car after opening and airing 15 minutes, 55 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Smoking room.....	+
	Drawing room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 8.....	+
	Berth, lower No. 4.....	—
<i>B. diphtheriæ</i>	Drawing room.....	+
	Smoking room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 6.....	+
	Berth, lower No. 10.....	+
<i>B. typhosus</i>	Drawing room.....	+
	Smoking room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 10.....	—
	Berth, lower No. 10.....	+
<i>B. subtilis</i>	Toilet room.....	+
	Smoking room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 7.....	+
	Berth, lower No. 4.....	+
<i>B. tuberculosis</i>	Floor of main sleeping compartment.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 86th day; increased 35 grams in weight; tuberculous lesions in liver, spleen.	
	Floor of main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 86th day; increased 70 grams in weight; tuberculous lesions in spleen, mesentery, lymph glands. Control guinea pig died of tuberculosis 50th day.	

The above experiment was done in the morning (8.25 to 10.25), at which time the relative humidity is high; but as the car had been artificially heated the night before the humidity was low. This probably accounts for the inefficient results obtained.

In the following experiment, temperature 46° F., polymerization was so marked that the deposit of paraform gave the interior furnishings of the car a frosty or white appearance.

EXPERIMENT NO. 54.

Formalin, 2,000 c. c., permanganate, 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Very cloudy, some melting snow on ground, no wind.

Temperature in car at beginning of experiment, 46° F.

Relative humidity in car at beginning of experiment, 45 per cent.

Time of exposure, 2 hours (11.25 a. m. to 1.25 p. m.).

Temperature in car after opening and airing 15 minutes, 47° F.

Relative humidity in car after opening and airing 15 minutes, 46 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 4.....	+
	Berth, lower No. 8.....	+
<i>B. diphtheriæ</i>	Floor main sleeping compartment.....	+
	Berth, upper No. 10.....	+
	Berth, lower No. 6.....	+
<i>B. yp osus</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 6.....	+
	Berth, lower No. 4.....	+
<i>B. subtilis</i>	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 6.....	+

As a rule, in this climate the relative humidity is higher at night than during the day, the reasons for which are obvious. The following three experiments were therefore done at nighttime of particularly dry days, and, as will be seen, gave better germicidal results than would have been obtained during the daytime.

To show this difference in humidity, the official relative humidity at 2 p. m. of the day on which these experiments were done is therefore given in each experiment.

This matter is of practical importance in comparatively dry climates, and shows the advantage of doing the work at nighttime. Of course still better results would be obtained by continuing the experiments until the next morning. However, the same results would not be obtained by starting the experiments during the day with a low humidity and continuing during the night, as much of the formaldehyde would be lost before the humidity was raised; and, furthermore, the car being closed, practically the only change in humidity in the car would be as a result of the fall in temperature during the night,

EXPERIMENT NO. 55.

Formalin, 2,000 c. c., permanganate, 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in main sleeping compartment and one in the alleyway at each end.

Weather: Clear, moon shining, very little breeze.

Temperature in car at beginning of experiment, 77° F.

Relative humidity in car at beginning of experiment, 69 per cent.

Time of exposure, 2 hours (8 p. m. to 10 p. m.).

Temperature in car after opening and airing 15 minutes, 72° F.

Relative humidity in car after opening and airing 15 minutes, 71 per cent.

Official relative humidity at 2 p. m. of the date on which the experiment was done, 26 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Drawing-room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 7.....	—
	Berth, lower No. 6.....	—
<i>B. diphtheriæ</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 10.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 8.....	—
	Berth, upper No. 11.....	—
<i>B. subtilis</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	+
	Berth, upper No. 8.....	+
	Berth, lower No. 9.....	+
<i>B. tuberculosis</i>	Floor main sleeping compartment.....	+
	Sputum exposed by Wilson method and injected into guinea pig; pig chloroformed 88th day; increased 115 grams in weight; lesions of tuberculosis in spleen, liver, lungs, and lymph glands.	
	Floor main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 88th day; increased but 5 grams in weight; lesions of tuberculosis in liver and spleen. Control guinea pig died of tuberculosis 63d day.	

EXPERIMENT NO. 56.

Formalin 2,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in main sleeping compartment and one in the alleyway at each end.

Weather: Clear, moon shining, no wind.

Temperature in car at beginning of experiment, 61.5° F.

Relative humidity in car at beginning of experiment, 64 per cent.

Time of exposure, 2 hours (8.35 p. m. to 10.35 p. m.).

Temperature in car after opening and airing 15 minutes, 57° F.

Relative humidity in car after opening and airing 15 minutes, 66 per cent.

Official relative humidity at 2 p. m. of the date on which the experiment was done, 39 per cent.

[+ means growth; - no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	-
	Smoking room.....	-
	Floor main sleeping compartment.....	-
	Berth, upper No. 4.....	-
	Berth, lower No. 9.....	+
<i>B. diphtheriæ</i>	Drawing-room.....	-
	Smoking room.....	-
	Floor main sleeping compartment.....	-
	Berth, lower No. 10.....	-
	Berth, upper No. 8.....	-
<i>B. typhosus</i>	Toilet room.....	-
	Smoking room.....	-
	Drawing-room.....	-
	Floor main sleeping compartment.....	-
	Berth, lower No. 6.....	-
<i>B. subtilis</i>	Drawing-room.....	+
	Smoking room.....	-
	Floor main sleeping compartment.....	-
	Berth, upper No. 5.....	+
	Berth, lower No. 4.....	+
<i>B. tuberculosis</i>	Floor main sleeping compartment.....	-
	Sputum exposed by Wilson method and injected into guinea pig; pig chloroformed 63d day; increased 270 grams in weight; no lesions of tuberculosis.	
	Floor main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 63d day; increased 150 grams in weight; lesions of tuberculosis in liver, spleen, and lymph glands. Control guinea pig died of tuberculosis 37th day.	

EXPERIMENT NO. 57.

Formalin 1,500 c. c., permanganate 750 grams, equally distributed in three iron buckets, one of which was placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear and moonshiny, no wind.

Temperature in car at beginning of experiment, 59° F.

Relative humidity in car at beginning of experiment, 57 per cent.

Time of exposure, 2 hours (8.40 p. m. to 10.40 p. m.).

Temperature in car after opening and airing 20 minutes, 55° F.

Relative humidity in car after opening and airing 20 minutes, 62 per cent.

Official relative humidity at 2 p. m. of the date on which the experiment was performed, 39 per cent.

[+ means growth; — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	+
	Berth, lower No. 6.....	+
<i>B. diphtheriæ</i>	Toilet room.....	—
	Smoking room.....	+
	Floor main sleeping compartment.....	—
	Berth, upper No. 5.....	—
<i>B. typhosus</i>	Berth, lower No. 10.....	—
	Smoking room.....	—
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
<i>B. subtilis</i>	Berth, upper No. 10.....	—
	Berth, lower No. 4.....	+
	Toilet room.....	+
	Smoking room.....	+
<i>B. tuberculosis</i>	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 4.....	+
	Floor main sleeping compartment.....	—
	Sputum exposed by the Wilson method and injected into guinea pig; pig chloroformed 63d day; increased 370 grams in weight; no lesions of tuberculosis.	
	Floor main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 63d day; increased 160 grams in weight; spleen, lungs, and lymph glands tuberculous.	
	Control guinea pig died of tuberculosis 37th day.	

II. DILUTED FORMALIN-PERMANGANATE METHOD.

The following four experiments were done with smaller quantities of formalin diluted with varying quantities of water before mixing with the permanganate. All except the first were done on comparatively dry days, with the object of determining whether the addition of the water would sufficiently increase the humidity to obtain efficient results on such days, as it has been satisfactorily demonstrated in previous experiments that moisture is one of the most essential factors in formaldehyde disinfection:

EXPERIMENT NO. 53.

Formalin 1,000 c. c., water 1,000 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, light southerly wind.

Temperature in car at beginning of experiment, 85° F.

Relative humidity in car at beginning of experiment, 73 per cent.

Time of exposure, 2 hours (11.30 a. m. to 1.30 p. m.).

Temperature in car after opening and airing 15 minutes, 88° F.

Relative humidity in car after opening and airing 15 minutes, 54 per cent.

[+ means growth, — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 6.....	—
<i>B. diphtheriæ</i>	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 6.....	—
	Berth, lower No. 8.....	—
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 10.....	—
<i>B. subtilis</i>	Smoking room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 6.....	+
<i>B. tuberculosis</i>	Smoking room.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 101st day; increased 200 grams in weight; marked lesions of tuberculosis in spleen and lymph glands, slight appearances in liver.	
	Floor main sleeping compartment.....	—
	Sputum exposed and injected into guinea pig; pig chloroformed 101st day; increased 240 grams in weight; no lesions of tuberculosis.	
	Control pig died of tuberculosis on 45th day.	

EXPERIMENT NO. 59.

Formalin 1,500 c. c., water 500 c. c., permanganate 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Dry and clear, light southwesterly wind.

Temperature in car at beginning of experiment, 76° F.

Relative humidity in car at beginning of experiment, 51 per cent.

Time of exposure, 2 hours (11.45 a. m. to 1.45 p. m.).

Temperature in car after opening and airing 15 minutes, 78° F.

Relative humidity in car after opening and airing 15 minutes, 36 per cent.

[+ means growth, — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 8.....	+
	Berth, upper No. 5.....	—
<i>B. diphtheriæ</i>	Toilet room.....	—
	Smoking room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 9.....	+
	Berth, lower No. 12.....	+
<i>B. typhosus</i>	Toilet room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 9.....	+
	Berth, lower No. 4.....	—
<i>B. subtilis</i>	Toilet room.....	—
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, lower No. 2.....	+
<i>B. tuberculosis</i>	Drawing-room.....	—
	Sputum exposed and injected into guinea pig; pig chloroformed 100th day; increased 270 grams in weight; no lesions of tuberculosis.	
	Floor main sleeping compartment.....	+
	Sputum exposed and injected into guinea pig; pig died of general tuberculosis on 88th day.	
	Control pig died of tuberculosis on 63d day.	

EXPERIMENT NO. 60.

Formalin 1,500 c. c., water 500 c. c., permanganate 1,000 grams, equally distributed in four galvan-
ized-iron buckets, two of which were placed in the main sleeping compartment of car and one in
the alleyway at each end.

Weather: Clear and dry with light southwesterly winds.

Temperature in car at beginning of experiment, 64° F.

Relative humidity in car at beginning of experiment, 45 per cent.

Time of exposure, 2 hours (11.35 a. m. to 1.35 p. m.).

Temperature in car after opening and airing 15 minutes, 69° F.

Relative humidity in car after opening and airing 15 minutes, 43 per cent.

[+ means growth, - no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	-
	Smoking room.....	+
	Drawing-room.....	-
	Floor main sleeping compartment.....	-
	Berth, upper No. 4.....	-
<i>B. dysenteriz</i>	Toilet room.....	-
	Smoking room.....	-
	Floor main sleeping compartment.....	+
	Berth, upper No. 2.....	-
	Berth, lower No. 7.....	+
<i>B. typhosus</i>	Smoking room.....	-
	Drawing-room.....	-
	Floor main sleeping compartment.....	+
	Berth, upper No. 6.....	+
<i>B. subtilis</i>	Berth, upper No. 10.....	+
	Smoking room.....	-
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
<i>B. tuberculosis</i>	Berth, upper No. 8.....	-
	Berth, lower No. 6.....	-
	Smoking room.....	-
	Sputum exposed and injected into guinea pig: pig chloro- formed 90th day: increased 300 grams in weight: no lesions of tuberculosis.	-
<i>B. tuberculosis</i>	Floor main sleeping compartment.....	-
	Sputum exposed and injected into guinea pig: pig chloro- formed 90th day: increased 300 grams in weight: no lesions of tuberculosis.	-
	Control pig died of tuberculosis on 63d day.	-

EXPERIMENT NO. 61.

Formalin, 1,500 c. c.; water, 500 c. c.; permanganate, 1,000 grams, equally distributed in four galvanized-iron buckets, two of which were placed in the main sleeping compartment of car and one in the alleyway at each end.

Weather: Clear, southerly wind.

Temperature in car at beginning of experiment, 79° F.

Relative humidity in car at beginning of experiment, 66 per cent.

Time of exposure, 2 hours (12 m. to 2 p. m.).

Temperature in car after opening and airing 15 minutes, 86° F.

Relative humidity in car after opening and airing 15 minutes, 53. per cent.

[+ means growth; —, no growth.]

Organism.	Place of exposure in car.	Result
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 11.....	—
<i>B. diphtheriæ</i>	Toilet room.....	—
	Smoking room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	—
	Berth, upper No. 8.....	+
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 10.....	—
	Berth, lower No. 6.....	—
<i>B. subtilis</i>	Smoking room.....	—
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 4.....	—
<i>B. tuberculosis</i>	Smoking room.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 100th day; increased 200 grams in weight; lesions of tuberculosis in spleen and lymph glands.	
	Floor main sleeping compartment.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 100th day; marked lesions of tuberculosis in liver and spleen. Control pig died of tuberculosis on 60th day.	

The results of the previous experiments done on dry days show that the organisms were usually not destroyed, and consequently no practical advantage gained by adding the water to the formalin. However, experiment No. 58 again proves our conclusions, namely, that successful disinfection does not depend so much upon the amount of gas as upon the temperature and humidity. Although a less quantity of formalin was used in this experiment than in the other three, the results were very much better.

III. RETORT WITHOUT PRESSURE.

A few experiments were done with this method, and as only one retort was used in each experiment, it was changed from one end of the car to the other at definite intervals during the process of vaporizing the formalin.

The locks of the car doors were removed in order to introduce the nozzle of the retort. The heat was under the retort 30 to 40 minutes before gas began to be given off, and then from 1 hour 30 minutes to 2 hours, depending upon temperature conditions in the different experiments, was required to completely vaporize the formalin. In one experiment, temperature 52° F., about 300 c. c. of liquid still remained in the retort at the end of the experiment. The time of exposure of the organisms was counted from the time of beginning to introduce the gas.

The experiments are as follows:

EXPERIMENT NO. 62.

Retort without pressure; formalin 2,000 c. c.

Time required to vaporize formalin, 1 hour 40 minutes.

Retort changed from one end of the car to the other every 20 minutes during process of vaporizing the formalin.

Weather: Damp and cloudy, light wind.

Temperature in car at beginning of experiment, 78° F.

Relative humidity in car at beginning of experiment, 71 per cent.

Time of exposure, 2 hours, from time of beginning to introduce the gas (11 a. m. to 1.00 p. m.)

Temperature in car after opening and airing 30 minutes, 81° F.

Relative humidity in car after opening and airing 30 minutes, 65 per cent.

[+ means growth; —, no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 8.....	—
	Berth, lower No. 6.....	—
<i>B. diphtheriæ</i>	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 4.....	—
	Berth, lower No. 10.....	—
<i>B. typhosus</i>	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 6.....	—
	Berth, lower No. 4.....	—
<i>B. subtilis</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	+
	Berth, upper No. 2.....	+
	Berth, lower No. 8.....	+
<i>B. tuberculosis</i>	Floor main sleeping compartment.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 90th day; increased 190 grams in weight; tuberculous lesions in spleen and lymph glands.	
	Floor main sleeping compartment.....	+
	Sputum exposed on carpet and injected into guinea pig; pig died of tuberculosis on 50th day. Control guinea pig died of tuberculosis on 60th day.	

EXPERIMENT NO. 63.

Retort without pressure; formalin 2,000 c. c.

Time required to vaporize formalin 1 hour and 30 minutes.

Retort changed from one end of car to the other every 15 minutes during process of vaporizing the formalin.

Weather: Dry and clear, light southwesterly wind.

Temperature in car at beginning of experiment, 73° F.

Relative humidity in car at beginning of experiment, 57 per cent.

Time of exposure, 2 hours, from time of beginning to introduce the gas (12 m. to 2 p. m.).

Temperature in car after opening and airing 15 minutes, 78° F.

Relative humidity in car after opening and airing 15 minutes, 38 per cent.

[+means growth; -, no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	-
	Drawing room.....	-
	Floor, main sleeping compartment.....	+
	Berth, upper No. 4.....	+
	Berth, lower No. 8.....	+
<i>B. diphtheriæ</i>	Drawing room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 8.....	+
	Berth, upper No. 10.....	-
	Berth, lower No. 12.....	+
<i>B. typhosus</i>	Toilet room.....	-
	Drawing room.....	-
	Floor, main sleeping compartment.....	+
	Berth, lower No. 7.....	-
<i>B. subtilis</i>	Toilet room.....	-
	Drawing room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 12.....	+
	Berth, lower No. 8.....	+
<i>B. tuberculosis</i>	Drawing room.....	+
	Sputum exposed and injected into guinea pig; pig chloroformed 97th day; marked lesions of tuberculosis in spleen.	
	Floor, main sleeping compartment.....	-
	Sputum exposed and injected into guinea pig; pig chloroformed 97th day; increased 300 grams in weight; no lesions of tuberculosis. Control guinea pig died of tuberculosis 63d day.	

EXPERIMENT No. 64.

Retort without pressure; formalin 2,000 c. c.

The process of vaporizing the formalin was continued for 2 hours, at the end of which time about 300 c. c. of fluid remained in the retort. During this time the retort was changed from one end of car to the other every 15 minutes.

Weather: Cloudy, melting snow, no wind.

Temperature in car at beginning of experiment, 52° F.

Relative humidity in car at beginning of experiment, 40 per cent.

Time of exposure, 2 hours, from time of beginning to introduce the gas (12 m. to 2 p. m.).

Temperature in car after opening and airing 15 minutes, 52° F.

Relative humidity in car after opening and airing 15 minutes, 40 per cent.

[+ means growth; —, no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	+
	Drawing room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 4.....	+
	Berth, lower No. 8.....	+
<i>B. diphtheriæ</i>	Floor, main sleeping compartment.....	+
	Berth, upper No. 10.....	+
	Berth, lower No. 6.....	+
<i>B. typhosus</i>	Toilet room.....	—
	Drawing room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 6.....	+
	Berth, lower No. 4.....	+
<i>B. subtilis</i>	Drawing room.....	+
	Floor, main sleeping compartment.....	+
	Berth, upper No. 6.....	+

With this method all the guinea pigs showed lesions of tuberculosis, one in experiment No 62 dying before the control. The others only showed a diminished virulence of the organism. Otherwise the results obtained in the above experiments agree rather closely with those in the formalin-permanganate method under similar conditions of temperature and humidity.

As much of the 2 hours is consumed in introducing the formaldehyde gas, doubtless more advantage would be gained by a longer exposure with this method than would be the case with the formalin-permanganate method. Although the temperature was 73° F., and humidity 57 per cent in experiment No. 63, the latter was not high enough to give efficient results. This indicates that about the same percentage of humidity is required in this method as in the formalin-permanganate method.

IV. AUTOCLAVE UNDER PRESSURE.

About 20 minutes were required to raise the pressure in the autoclave to 60 pounds. The pressure was kept between 40 and 60 pounds while vaporizing the formalin. This process required from 40 to 60 minutes in the different experiments, after which practically no liquid remained in the autoclave.

During this process the autoclave was changed from one end of the car to the other every 10 or 15 minutes. As with the retort, it was necessary to remove the locks from the doors in order to introduce the nozzle of the autoclave.

The experiments are as follows:

EXPERIMENT NO. 65.

Autoclave, formalin 2 000 c. c.

Time required to vaporize formalin, 45 minutes.

Autoclave changed from one end of car to other every 15 minutes during process of vaporizing the formalin.

Weather: Clear; southerly breeze.

Temperature in car at beginning of experiment, 78° F.

Relative humidity at beginning of experiment, 67 per cent.

Time of exposure, 2 hours (11.55 a. m. to 1.55 p. m.) from time of beginning to introduce the gas.

Temperature in car after opening and airing 30 minutes, 87° F.

Relative humidity after opening and airing 30 minutes, 50 per cent.

[+ means growth; —, no growth].

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, upper No. 8.....	—
<i>B. diphtheriæ</i>	Toilet room.....	—
	Smoking room.....	—
	Floor main sleeping compartment.....	+
	Berth, upper No. 8.....	—
	Berth, lower No. 4.....	+
<i>B. typhosus</i>	Toilet room.....	—
	Smoking room.....	—
	Drawing-room.....	—
	Floor main sleeping compartment.....	—
	Berth, lower No. 10.....	—
<i>B. subtilis</i>	Smoking room.....	—
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 6.....	—
<i>B. tuberculosis</i>	Smoking room.....	—
	Sputum exposed and injected into guinea pig. Pig chloroformed 100th day—increased 270 grams in weight; no lesion of tuberculosis.	+
	Floor main sleeping compartment.	
	Sputum exposed and injected into guinea pig. Pig chloroformed 100th day—increased 140 grams in weight; only the spleen showed lesions of tuberculosis.	
	Control guinea pig died of tuberculosis 60th day.	

EXPERIMENT NO. 66.

Autoclave, formalin 2,000 c. c.

Time required to vaporize formalin, 40 minutes.

Autoclave changed from one end of car to other every 10 minutes during the process of vaporizing the formalin.

Weather: Clear; very little wind.

Temperature in car at beginning of experiment, 74.5° F.

Relative humidity at beginning of experiment, 64 per cent.

Time of exposure, 2 hours (11.35 a. m. to 1.35 p. m.) from time of beginning to introduce the gas.

Temperature in car after opening and airing 25 minutes, 83° F.

Relative humidity after opening and airing 25 minutes, 40 per cent.

[+ means growth: —, no growth].

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, lower No. 8	—
<i>B. diphtheriæ</i>	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, upper No. 9	—
	Berth, lower No. 6	—
<i>B. typhosus</i>	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor main sleeping compartment	—
	Berth, lower No. 10	—
<i>B. subtilis</i>	Toilet room	—
	Smoking room	+
	Floor main sleeping compartment	+
	Berth, upper No. 7	—
<i>B. tuberculosis</i>	Berth, lower No. 3	+
	Floor main sleeping compartment	—
	Sputum exposed by Wilson method and injected into guinea pig. Pig chloroformed 95th day—increased 410 grams in weight; no lesions of tuberculosis.	
	Floor main sleeping compartment	+
	Sputum exposed on carpet and injected into guinea pig. Pig died of tuberculosis 59th day.	
	Control guinea pig died of tuberculosis 60th day.	

EXPERIMENT NO. 67.

Autoclave, formalin 2,000 c. c.

Time required to vaporize formalin, 50 minutes.

Autoclave changed from one end of car to other every 10 minutes during the process of vaporizing the formalin.

Weather: Cloudy; moderate northeast wind.

Temperature in car at beginning of experiment, 47° F.

Relative humidity at beginning of experiment, 53 per cent.

Time of exposure, 2 hours (12.25 p. m. to 2.25 p. m.) from time of beginning to introduce the gas

Temperature in car after opening and airing 15 minutes, 40° F.

Relative humidity after opening and airing 15 minutes, 52 per cent.

[+ means growth; —, no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 12.....	+
	Berth, lower No. 8.....	+
<i>B. diphtheriæ</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 11.....	+
<i>B. typhosus</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 7.....	+
	Berth, lower No. 3.....	+
<i>B. subtilis</i>	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 1.....	+
	Berth, lower No. 4.....	+

The above results do not differ materially from those with the other methods described above. For comparison, experiments Nos. 46 and 66 were done simultaneously, as were No. 61 and 65. Of the four guinea pigs used in this method two showed no lesions of tuberculosis, while the other two showed that the virulence of the organism had been diminished as compared with the controls.

A longer exposure would no doubt have given better results, especially in experiments Nos. 65 and 66. Evidently about the same temperature and humidity are required in this method to accomplish efficient disinfection as in the other methods.

V. GENERATING LAMP.

Two lamps were used in an experiment, placed one in either end of the main compartment of the sleeping car. Fifteen hundred c. c. of commercial wood alcohol were used in each lamp.

The lamps were started, as previously described (p. 57), in the room experiments. As soon as they began to give off formaldehyde gas, etc., the car was closed and the time of exposure of the organisms

counted from that time. At the conclusion of the experiments the process of oxidation of the alcohol seemed to be completed except in experiment No. 71. In this experiment, temperature 50° F., both lamps were still burning at the end of 2 hours.

EXPERIMENT NO. 68.

Two generating lamps; commercial wood alcohol 3,000 c. c. (1,500 c. c. in each lamp).^a

Lamps placed one in each end of main sleeping compartment of car.

Weather: Damp and cloudy, light wind.

Temperature in car at beginning of experiment, 77° F.

Relative humidity in car at beginning of experiment, 71 per cent.

Time of exposure, 2 hours (11.40 a. m. to 1.40 p. m.) from time of starting lamps and closing car.

Temperature in car after opening and airing 20 minutes, 81° F.

Relative humidity in car after opening and airing 20 minutes, 72 per cent.

[+ means growth, — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	—
	Smoking room	—
	Floor, main sleeping compartment	—
	Berth, upper No. 5	—
	Berth, lower No. 8	—
<i>B. diphtheriæ</i>	Smoking room	—
	Drawing-room	—
	Floor, main sleeping compartment	+
	Berth, upper No. 4	—
<i>B. typhosus</i>	Berth, lower No. 4	—
	Toilet room	—
	Smoking room	—
	Drawing-room	—
	Floor, main sleeping compartment	—
<i>B. subtilis</i>	Berth, lower No. 9	—
	Smoking room	+
	Drawing-room	+
	Floor, main sleeping compartment	+
	Berth, upper No. 7	+
<i>B. tuberculosis</i>	Berth, lower No. 6	+
	Floor, main sleeping compartment	+
	Sputum exposed by Wilson method and injected into guinea pig; pig chloroformed 90th day; increased 230 grams in weight; tubercular lesions in liver, spleen.	
	Floor, main sleeping compartment	+
	Sputum exposed on carpet and injected into guinea pig; pig chloroformed 90th day; increased 100 grams in weight; marked lesions of tuberculosis in liver, spleen, lungs, diaphragm, and lymph glands.	
	Control guinea pig died of tuberculosis 60th day.	

^a In experiments Nos. 68, 69, 70 and 71, the quantity of wood alcohol was about 10 per cent less than is required by U. S. Quarantine regulations.—[ED.]

EXPERIMENT NO. 69.

Two generating lamps; commercial wood alcohol 3,000 c. c. (1,500 c. c. in each lamp).

Lamps placed one in each end of main sleeping compartment of car.

Weather: Clear and dry, very little wind.

Temperature in car at beginning of experiment, 60° F.

Relative humidity in car at beginning of experiment, 58 per cent.

Time of exposure, 2 hours (11.30 a. m. to 1.30 p. m.) from time of starting lamps and closing car.

Temperature in car after opening and airing 15 minutes, 62° F.

Relative humidity in car after opening and airing 15 minutes, 50 per cent.

[+ means growth, — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	—
	Smoking room.....	+
	Floor, main sleeping compartment	+
	Berth, upper No. 4.....	+
	Berth, lower No. 10.....	—
<i>B. diphtheriæ</i>	Smoking room.....	+
	Drawing-room.....	+
	Floor, main sleeping compartment	+
	Berth, upper No. 6.....	+
	Berth, lower No. 5.....	+
<i>B. typhosus</i>	Toilet room.....	+
	Drawing-room.....	+
	Floor, main sleeping compartment	—
	Berth, upper No. 3.....	—
	Berth, lower No. 12.....	+
<i>B. subtilis</i>	Smoking room.....	+
	Drawing-room.....	+
	Floor, main sleeping compartment	+
	Berth, upper No. 10.....	+
	Berth, lower No. 6.....	+
<i>B. tuberculosis</i>	Floor, main sleeping compartment	+
	Sputum exposed by Wilson method and injected into guinea pig; pig chloroformed 63d day; increased 175 grams in weight; tubercular lesions in liver, spleen, and lymph glands.	
	Floor, main sleeping compartment	+
	Sputum exposed on carpet and injected into guinea pig; pig died of tuberculosis on 50th day. Control guinea pig died of tuberculosis 37th day.	

EXPERIMENT NO. 70.

Two generating lamps; commercial wood alcohol 3,000 c. c. (1,500 c. c. in each lamp).

Lamps placed one in each end of main sleeping compartment of car.

Weather: Clear and dry, light southwesterly breeze.

Temperature in car at beginning of experiment, 65° F.

Relative humidity in car at beginning of experiment, 48 per cent.

Time of exposure, 2 hours (11.15 a. m. to 1.15 p. m.) from time of starting lamps and closing car.

Temperature in car after opening and airing 10 minutes, 69° F.

Relative humidity in car after opening and airing 10 minutes, 39 per cent.

[+ means growth, — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room	+
	Smoking room	+
	Drawing-room	+
	Floor main sleeping compartment	+
	Berth, lower No. 6	+
<i>B. diphtheriæ</i>	Toilet room	+
	Smoking-room	+
	Drawing-room	+
	Floor main sleeping compartment	+
	Berth, lower No. 4	+
<i>B. typhosus</i>	Toilet room	—
	Smoking room	+
	Drawing-room	+
	Floor main sleeping compartment	+
	Berth, upper No. 3	+
<i>B. subtilis</i>	Smoking room	+
	Drawing-room	+
	Floor main sleeping compartment	+
	Berth, upper No. 7	+
	Berth, lower No. 8	+
<i>B. tuberculosis</i>	Smoking room	+
	Sputum exposed and injected into guinea pig; pig chloroformed 96th day; increased 300 grams in weight; tubercular lesions in spleen.	
	Floor main sleeping compartment	+
	Sputum exposed and injected into guinea pig; pig chloroformed 96th day; increased 230 grams in weight; liver, spleen, and lymph glands show lesions of tuberculosis.	
	Control guinea pig died of tuberculosis 63d day.	

^a In experiments Nos. 68, 69, 70 and 71, the quantity of wood alcohol was about 10 per cent less than is required by U. S. Quarantine regulations.—[Ed.]

EXPERIMENT NO. 71.

Two generating lamps; commercial wood alcohol 3,000 c. c. (1,500 c. c. in each lamp).

Lamps placed one in each end of main sleeping compartment of car.

Weather: Cloudy, moderate northeast wind.

Temperature of car at beginning of experiment, 50° F.

Relative humidity of car at beginning of experiment, 55 per cent.

Time of exposure, 2 hours (12.30 p. m. to 2.30 p. m.), from time of starting lamps and closing car.

Temperature in car after opening and airing 10 minutes, 45 ° F.

Relative humidity in car after opening and airing 10 minutes, 57 per cent.

[+ means growth, — no growth.]

Organism.	Place of exposure in car.	Result.
<i>B. coli communis</i>	Toilet room.....	+
	Smoking room.....	+
	Drawing-room.....	+
	Floor main sleeping compartment.....	+
	Berth, lower No. 10.....	+
<i>B. diphtheriæ</i>	Toilet room.....	+
	Smoking room.....	+
	Berth, upper No. 10.....	+
<i>B. typhosus</i>	Toilet room.....	+
	Smoking room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 2.....	+
	Berth, lower No. 6.....	+
<i>B. subtilis</i>	Toilet room.....	+
	Smoking room.....	+
	Floor main sleeping compartment.....	+
	Berth, upper No. 8.....	+

The results in experiment No. 68 are satisfactory except that the tubercle bacilli were not killed, although their virulence was diminished. In the other experiments most of the organisms escaped destruction, due no doubt to the low relative humidity and temperature.

In all the experiments with this method it was possible to enter the car almost as soon as it was opened. Consequently, no special advantage would likely have been gained by a longer exposure in the above experiments. Although this method increased the humidity considerably, it did not do so sufficiently in experiment No. 69 (humidity 58 per cent) to accomplish efficient results.

SUMMARY AND CONCLUSIONS.

Formaldehyde gas, regardless of the method by which it is evolved, is a powerful surface disinfectant under certain conditions. Successful disinfection with it is so dependent upon several factors that its usefulness is more or less limited. The temperature and humidity are of primary importance, while the influence of the winds, character of the room, etc., are of secondary importance.

The effects of temperature seem to be principally upon the state of the formaldehyde after it is liberated: that is, below a certain point it polymerizes. This seems to take place below about 65° F. with the formalin-permanganate and below about 60° F. with the other methods. Although the germicidal power of formaldehyde is not entirely lost at these temperatures, it is so diminished as to be of very little practical value for disinfection purposes.

The rôle played by the relative humidity in formaldehyde disinfection is more important than that of any other other influencing factors. In the absence of moisture, formaldehyde is practically inert as a germicide. The minimum percentage of relative humidity that invariably gives efficient results in disinfecting with formaldehyde can not be stated exactly, since it varies slightly according to other conditions, such as temperature, wind, the quantity of gas present, the space to be disinfected, etc.

However, it appears from experience that the relative humidity in the air before starting an experiment should not be lower than as follows: (1) For an ordinary well-closed room, 60 per cent; (2) for ordinary railway cars, 65 per cent. With a high temperature, a large quantity of formaldehyde, and a long exposure, efficient results may be obtained with slightly lower percentages of humidity than just stated.

There is not much difference in the amount of moisture given off by the different methods. This form of moisture, however, does not seem to answer for disinfection purposes so well as the natural humidity in the atmosphere. This conclusion is indicated in some experiments in which the relative humidity before starting the experiment was below the point above stated, and while the moisture given off raised the percentage of humidity to a point where efficient results would be expected, the organisms usually escaped destruction. Consequently, the exact value of the moisture given off in the process of liberating the formaldehyde can not be positively stated, but it appears that too much trust must not be placed in it.

In the experiments in a bottle very good results were obtained with a relative humidity between 50 and 60 per cent, which is slightly less than that required in the room and car experiments. Of course, the conditions in the bottle were much more favorable for efficient results than usually obtain in ordinary formaldehyde disinfection.

The results of our chemical determinations must be interpreted as representing the quantities of formaldehyde gas that may be expected to be present in a fairly air-tight room when charged with 600 c. c. of formalin by the various methods described and after a certain interval of time which varies with the method used.

According to the maximum quantity of gas found, on an average warm day and regardless of the time required to evolve it, the methods may be arranged as follows:

	Per cent.
Retort without pressure	47.0
Autoclave	41.5
Formalin-permanganate	39.15
Diluted formalin-permanganate	35.1
Sheet spraying	30.48
Formalin-aluminum sulphate-lime	14.0

The above figures simply represent the percentage of formaldehyde gas found, as compared with the quantity contained in the amount of formalin used in an experiment.

As alcohol is used in the generating lamp, it is impracticable at this time to compare the percentage of formaldehyde evolved by this method with that evolved by the above methods.

Under conditions as given above the methods may be arranged according to the maximum quantity of formaldehyde gas actually found per cubic foot of air space in the room, as follows:

	Grams.
Retort without pressure	0.05037
Autoclave	0.04448
Formalin-permanganate	0.0419
Diluted formalin-permanganate	0.03755
Sheet spraying	0.03262
Formalin-aluminum sulphate-lime	0.01498

Below a temperature of about 65° F. for the formalin-permanganate and about 60° F. for the other methods polymerization or other change in the formaldehyde takes place to such an extent that only a relatively small percentage of gas is obtained. This of course is more marked the lower the temperature.^a

The different methods are affected in about the same proportion except in case of the sheet-spraying method. In this latter method it seems that the formaldehyde is not even given off when the temperature is below the point above stated. In the different experiments in the bottle with the formalin-permanganate method the percentages of formaldehyde liberated agree fairly well, but are slightly lower than in the room experiments under similar conditions of temperature. The difference is due in all probability to the small quantities of substances used in the former experiments.

The bottle experiments show that a low temperature does not materially affect the quantity of formaldehyde actually given off, and therefore the small percentages obtained in the room under this condition are principally due to the formaldehyde undergoing change after liberation.

^a This polymerization, however, does not take place in the gas, as evolved by the formaldehyde generating lamp, the product of which does not seem to polymerize under any conditions of temperature at which experiments have, up to this time, been conducted.—[ED.]

A small quantity of formaldehyde is efficient for surface disinfection, provided the temperature and humidity are high. A large quantity assists penetration, as also do high temperature and humidity; but even then the penetrating power of formaldehyde is so limited that it should not be employed for disinfection purposes requiring any marked degree of penetration.

Depending upon the conditions as stated, the quantity of formalin may vary from 200 to 500 c. c. per 1,000 cubic feet of air space. As sleeping cars have many ventilators, etc., the leakage of formaldehyde gas from them is quite rapid, so that it is necessary to use a relatively larger quantity of formalin than is usually required in room disinfection.

The length of exposure depends upon circumstances. Two hours under favorable conditions were usually sufficient in our experiments. In the car experiments very little formaldehyde gas was found in the car at the end of this time. Consequently very little would have been gained by a longer exposure. In a well-closed room a longer exposure would doubtless be of advantage, although our conclusions are that in surface disinfection with formaldehyde the organisms are mostly killed within the first hour of exposure if they are destroyed at all.

For simplicity and rapidity the formalin-permanganate method is far superior to any of the other methods tried. It liberates the formaldehyde gas almost instantaneously and in almost as large quantities as the retort and autoclave methods.

Better disinfection is accomplished by having a comparatively large quantity of formaldehyde gas and a short exposure than a small quantity and long exposure. The formalin-permanganate method is more applicable than any of the other methods for disinfecting an inclosure which is not comparatively tight. With this method a larger percentage of exposures of *B. tuberculosis* were killed than with any of the other methods.

The formalin and permanganate should be used in about the proportion of 1 c. c. of the former to 0.5 gram of the latter. No obvious advantage is gained by adding water to the formalin before mixing with the permanganate.

The retort, autoclave, and generating lamp are efficient methods under favorable conditions, but they require more or less complicated apparatus, as well as considerable time to evolve the formaldehyde gas.

The sheet-spraying method is rather simple and economical and is especially applicable for disinfection purposes requiring long exposure.

The formalin-aluminum sulphate-lime method is not so simple and efficient as some of the other methods, but under favorable conditions it may be used with very good results.

TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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A STATISTICAL STUDY OF THE PREVALENCE
OF INTESTINAL WORMS IN MAN.

BY

CH. WARDELL STILES

AND

PHILIP E. GARRISON.



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A STATISTICAL STUDY OF THE PREVALENCE OF INTESTINAL WORMS IN MAN.

By CH. WARDELL STILES, Ph. D., Chief of Division, and PHILIP E. GARRISON,^a A. B., M. D.,
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SUMMARY.

In order to determine the frequency and the species of intestinal worms present in man in at least two localities in the United States and to bring out other facts relating to the presence of worms in the human intestine, we have examined 3,457 persons. These persons were inmates of the United States Government Hospital for the Insane (St Elizabeth) and of an orphanage, both of which are in the District of Columbia, and of the Connecticut Hospital for the Insane at Middletown, Conn.

Of the 3,457 persons, 349 were infected with intestinal worms, an average of 10.10 per cent; 35 of the 349 infected persons harbored 2 species of parasites, and 1 person was infected with 3 species, making a total of 386 infections, or an average of 11.17 infections per 100 persons.

Seven species of worms were found. They occurred in the following order of frequency: Whipworms, *Trichuris* (7.69 per cent), pinworms, *Oxyuris* (1.30 per cent), hookworms (1.04 per cent), eelworms, *Ascaris* (0.49 per cent), dwarf tapeworms, *Hymenolepis nana* (0.35 per cent), Cochin China worms, *Strongyloides* (0.23 per cent), beef tapeworms, *Tænia saginata* (0.06 per cent).

The rates of infection found among our cases for whipworms, pinworms, eelworms, and for beef tapeworms are, in general, much lower than the rates reported for these parasites from other similar investigations; the minimum, maximum, and average rates of infection for these species, compiled from all the statistical data on the subject at our command (other than our own investigations), are, respectively, as follows: Whipworms, 2.31 per cent, 89.65 per cent, 12.69 per cent; pinworms, 0.07 per cent, 30.16 per cent, 7.24 per cent; eelworms, 5.83 per cent, 37.39 per cent, 16.35 per cent; beef tapeworms, 0.07 per cent, 3.66 per cent, 0.40 per cent.

Of the 36 infections with hookworms, 21 occurred in persons admitted to the Government Hospital from distant localities, and 14 of these infections in soldiers returned from service in the Philippine Islands. That the dwarf tapeworm should present 12 infections among our cases and the beef tapeworm only 2 is contradictory to the generally accepted opinion regarding the relative frequency of these cestodes in this country. Eleven of the 12 infections with the dwarf tapeworm occurred in males, 6 of the 12 in male children, and 5 of the 12 in male negroes.

^aCommissioned in U. S. Navy as Assistant Surgeon, June, 1906.

^bIn making these numerous examinations we have been assisted by Arthur L. Murray, M. D., David G. Willets, Ph. B., Brayton H. Ransom, M. A., Earl C. Stevenson, M. D., and William F. Hemler, M. D.

Our total rate of infection with all intestinal worms among the 3,457 persons examined is lower than that reported from a similar investigation by any other author.

The 459 negroes among our cases showed an average of 12.42 infections per 100 persons. A group of 746 white persons having similar histories and from the same locality gave an average of 4.96 infections per 100 persons. The higher rate of infection among the negroes is especially marked in the case of whipworms and dwarf tapeworms.

The 2,311 males among the 3,457 persons examined gave an average of 10.68 infections per 100 persons; the 1,146 females gave an average of 12.13 infections per 100 persons. A higher rate of infection among females than among males is found in the results of almost all other similar investigations, and the total average rates of infection with intestinal worms for the two sexes from the combined statistics (except our own) of all authors available to us are: Males, 33.47 infections per 100 persons; females, 44.58 infections per 100 persons. The higher rate of infections found among males than among females in the 2,324 patients examined at the Government Hospital is explained by the presence of over 205 males admitted from tropical and subtropical service in the United States Army, who show about 35 infections per 100 persons.

The rates of infection with whipworms, eelworms, and beef tapeworms are higher among the females than are the rates for each of these parasites among the males. The greatest difference between the sexes appears in the case of the whipworm, the rates being 6.45 and 10.21 per cent, respectively, for males and females. Pinworms, hookworms, Cochin China worms, and dwarf tapeworms each present a higher rate of infection among males. The higher rate of infection among males is most marked in the case of the dwarf tapeworm. From the combined statistics of all other investigations at our command the greater prevalence among females than among males seems to hold for each species of intestinal worm, except dwarf tapeworm, so far as reported. For hookworms and Cochin China worms no percentage statistics are available regarding the relative prevalence in the two sexes. The one statistical report we have of the frequency of dwarf tapeworms shows a higher rate of infection with this parasite among male children than among female children.

The 3,325 persons among the 3,457 persons examined whose ages could be obtained were divided into four age groups, namely, those under 15 years of age, those from 15 to 30 years of age, those from 31 to 50 years of age, and those 51 years of age and older. The rate of infection with intestinal worms in each of these groups was as follows: Under 15 years, 21.14 infections per 100 persons; 15 to 30 years, 15.73 infections per 100 persons; 31 to 50 years, 11.41 infections per 100 persons; 51 years and older, 7.06 infections per 100 persons. Whipworms and eelworms are the only parasites which, when taken separately, showed a tendency to a gradual decrease in frequency as we pass from the younger to the older groups; pinworms showed little variation at different ages; hookworms showed by far their highest rate among persons from 15 to 30 years of age, namely, in the group containing most of the soldiers returned from service in the Philippine Islands; with this exception the rate of infection with this parasite tended to decrease consistently as the age of the patients advanced. Cochin China worms progressively increased in frequency as we pass from the younger to the older age groups; the dwarf tapeworm showed 4.88 per cent of infections among persons under 15 years of age, no infections among those from 15 to 30 years, and only 0.30 and 0.16 per cent, respectively, in the two succeeding groups; the two infections with fat tapeworms occurred one in each of the two older groups. A summary of the statistics of other authors regarding the relative frequency of whipworms, eelworms, and pinworms among persons of different ages indicates a much higher rate of infection with each of these parasites among persons under 15 years old than among persons above that age; the maximum rates of infection with whipworms and eelworms appear among children from 5 to 15 years old, and with pinworms at a still earlier age.

The 3,334 persons examined at the United States and the Connecticut hospitals were divided, according to the length of time they had been in the hospital, into 5 groups, namely, patients of less than 1 year's hospital residence, from 1 to 3 years, from 4 to 8 years, from 9 to 15 years, and those of more than 15 years' hospital residence. These groups presented,

respectively, the following rates of infection with intestinal worms: Less than 1 year's residence, 12.46 infections per 100 persons; 1 to 3 years, 10.84 infections per 100 persons; 9 to 15 years, 9.66 infections per 100 persons; more than 15 years' residence, 12.99 infections per 100 persons. The rate of infection with whipworms varied in the different groups in much the same manner as did the rate for all infections; pinworms showed a consistent tendency to increase in frequency, and hookworms a consistent tendency to decrease in frequency, with prolonged institutional life; eelworms presented their highest rate of infection among persons of less than 1 year's residence, and Cochin China worms among those of more than 15 years' residence, but neither parasite shows any consistent variation throughout the 5 groups.

A mathematical explanation of the variations in the amount of infection found among persons of different lengths of institutional life can be given only when the longevity of the parasite and the amount of infection endemic within the hospital are known. It would appear that the tendency is for high entrance infections to be lowered and low entrance infections to be increased until the percentage of endemic infection is reached, namely, until the endemic infection exactly balances the mortality of the parasites.

Among the 3,334 adults examined, 1,023 (white) who were of foreign birth gave an average of 11.44 infections per 100 persons; 1,637 native-born whites gave an average of 9.35 infections per 100 persons. Whipworms, eelworms, and the fat tapeworms gave higher rates of infection among the foreign born; pinworms, hookworms, and Cochin China worms gave higher rates among the native born. Among the foreign-born patients, those of German birth gave an average of 7.36 infections per 100 persons; the English born, an average of 10.13 infections per 100 persons; the Irish born, an average of 13.68 infections per 100 persons.

Two hundred and fifty-six persons (white and negro) admitted to the Government Hospital from the District of Columbia (chiefly from city life) within 1 year prior to examination gave an average of 8.20 infections with intestinal worms; 108 persons (white) admitted to the Connecticut Hospital from Connecticut (rural and city life) within 1 year prior to examination gave an average of 9.26 infections per 100 persons; 148 white persons admitted to the Government Hospital from the District of Columbia (chiefly from city life) gave an average of 5.41 infections per 100 persons. That the higher rate of infection among persons admitted from Connecticut is due to the fact that they were in part admitted from rural life is rendered very probable in that among the 26 of the 108 persons, admitted from Connecticut, who had an assured history of city life the rate of infection was only 3.84 per 100.

The 1,494 white males examined at the Government Hospital were divided, according to their history prior to admission, into 6 groups, namely, old soldiers admitted from the various Soldiers' Homes, civilians from the District of Columbia, soldiers from the regular United States army posts before 1898, sailors from the United States Navy, soldiers from active service or the special reserve camps after 1898, and soldiers admitted from service in the Philippine Islands. These groups showed, respectively, the following rates of infection with intestinal worms: Old soldiers, 3.80 infections per 100 persons; civilians, 5.54 per 100 persons; soldiers from the Army prior to 1898, 7.26 per 100 persons; sailors, 8.74 per 100 persons; soldiers from the Army after 1898, 21.11 per 100 persons; soldiers from Philippine service, 45.22 infections per 100 persons. The rate of infection with whipworms varied in the different groups in about the same manner as did the rate for all parasites; the pinworm gave its highest rate of infection among soldiers admitted from the Army before 1898, its next highest among the old soldiers from the Soldiers' Homes, and it did not appear among the soldiers returned from the Philippine Islands; hookworms presented by far their highest rate of infection (12.17 per cent) among the Philippine soldiers and their next highest (3.33 per cent) among the soldiers admitted from the Army after 1898.

The infections with intestinal worms found among our cases were very unevenly distributed among the different buildings, sections of buildings, and wards of the two hospitals from which the adult subjects of our examinations were taken. At the Government Hospital

an uneven distribution might be explained by the difference in the histories of the patients prior to admission, especially as patients of a similar history are often found congregated upon the same ward or in the same building. At the Connecticut Hospital the patients have a relatively uniform history, having been admitted from civil life and from the bounds of the one State. At the Connecticut Hospital 13 wards gave no infections; 29 wards varied from 2.86 to 75 infections per 100 persons. The rate of infection in the four buildings varied from 5 infections per 100 persons in building A to 61.33 infections per 100 persons in building D: separating the male and the female sections in each building, we have 7 sections, among which the rate of infection varied from 2.56 to 61.33 per 100 persons.

The same unequal distribution of infections among the different wards was found in the case of pinworms and of whipworms, considered separately. With regard to pinworms, this is naturally explainable by the direct transmissibility of the parasite from one person to another: hence we would find a group of cases centered around one focus of infection. In the absence of direct transmissibility in the case of whipworms, we have analyzed the conditions of sex, age, length of hospital residence, and of nativity among the patients upon the different wards with a view to discovering such combination of these factors as would explain the widely varying amounts of infection. No combination was found which would give any adequate explanation.

Reports on the examination of over 25,000 persons for intestinal worms in different parts of the world, published by over 30 different authors, bring out the fact that the rate of infection varies widely in different localities.

Our statistics of the relative frequency of whipworms among whites and negroes in the District of Columbia, when compared with the statistics of the relative frequency of typhoid in the two races in this District, are not in harmony with the theory that whipworms play a rôle in typhoid fever. The point remains to be established, however, whether the published statistics as to the frequency of typhoid in the negro and in the white are not misleading, in view of the fact that the published lethality of typhoid is so much higher in the negro than it is in the white.

INTRODUCTION.

The present investigation was undertaken for the purpose of determining the prevalence of intestinal worms in man in certain localities in the United States. Heretofore our ideas on this subject have been based chiefly upon the number of infections reported by general practitioners and by hospital clinicians in our own country, or drawn by analogy from the results of foreign investigations. Foreign results, however, are not necessarily applicable to this country; further, the conclusions founded upon the reports of physicians and hospitals are naturally inadequate when we consider that, as a rule, only the severer cases of infection are brought to the notice of the physician; furthermore, that usually only the most common worms are considered by practitioners, and, finally, when we recognize the fact that as a rule microscopic examination of the feces, which in most instances is preeminently the best and in many cases the only certain method of diagnosing intestinal infections with animal parasites, has until within the last few years had little place in the practice of American physicians or even in American hospitals.

SOURCE OF MATERIAL.—The practical difficulties in the way of obtaining several thousand specimens of feces from the general population can be appreciated even by persons who have not had expe-

rience in this kind of work. It was realized at the outset that in order to have a broad basis for our study it would be necessary to turn to large institutions where people were gathered under such control as would make it possible to obtain specimens in sufficiently large numbers and under properly governed conditions.

The Government Hospital for the Insane, in the District of Columbia, offered a convenient and favorable field for the investigation, and in September, 1902, it was arranged with Dr. A. B. Richardson, late superintendent, that we should examine the patients of that institution. These courtesies were continued after Doctor Richardson's death by Acting Superintendent Dr. M. J. Stack, and later by Dr. W. A. White, Doctor Richardson's successor.

Invitations were subsequently received to take up the work in a number of institutions in various parts of the country. It was decided to accept that of the Connecticut Hospital for the Insane at Middletown, Conn., and during the summer of 1903 specimens from over 1,000 of the patients were examined. Desiring to obtain data for children, arrangements were made with an orphanage in the District of Columbia by which we examined 123 inmates of the institution.

It was fully realized that in selecting these fields for our investigation we were departing from the normal conditions of life found in the general population and that this departure might introduce certain elements which would modify our results. It undoubtedly has done so. Nevertheless, from facts brought out in the investigation itself, we consider that the results obtained are of value not only as indicating the frequency and distribution of intestinal worms among the classes of patients actually studied, but that these results, though very complicated, will, properly interpreted, serve as a fair indication of the presence of helminthiasis in the population at large in the New England and the Middle Atlantic States.

SCOPE OF THE WORK.—Our aim primarily was to determine the frequency of the different species of intestinal worms in man in the localities in question. At the same time we have endeavored to ascertain any conditions among our cases which might have any relation to the presence of worms in the intestine. For this purpose as full data as possible were taken from the records of the patients examined, including race, sex, age, nativity, occupation, residence, and length of institutional life. We have considered also the distribution of the infections upon the wards of the hospitals. Finally there is appended a summary of the results of other statistical researches into the prevalence of worms in the human intestine and a brief consideration of the relative prevalence of whipworms among the whites and negroes in the District of Columbia with regard to the occurrence of typhoid fever in the two races.

METHOD OF EXAMINATION.—The method used for diagnosis throughout the investigation has been that of microscopic examination of the feces for the eggs, larvæ, or adult forms of the parasites. The examinations were made as thorough as possible by studying not less than 10 cover-glass preparations of each fecal specimen and by having at least two men work independently on each set of preparations. Careful measures were taken to prevent mutual or outside contamination of the specimens during their collection and examination.

As is generally recognized, microscopic examination of the feces is an uncertain method of diagnosing the presence of the pinworm. Therefore only minimum statistics can be claimed for our figures for this parasite, the possibility being present that the number of infections was greater than actually found. It is possible, also, that the eggs of certain tapeworms, especially of *Tænia*, are not constantly present in the stools in the case of an infection with these parasites. The ova of some nematode worms have been said to disappear temporarily from the feces during an infection, but probably such disappearance would be exceptional and due to special conditions, as when the patient is under anthelmintic or purgative treatment or perhaps when he indulges unduly in some food or drink or takes some drug which has a stupefying effect on the parasites.

The possible temporary absence of ova in the feces of persons infected with intestinal worms should, of course, be taken into account in considering the results of our own work as well as the results of all other investigations of a similar nature conducted by examination of the feces. Such a possibility could be guarded against only by repeated examinations of each patient, which, if the work were on a large scale, would necessarily mean to narrow the basis of the investigation, that is, to examine fewer patients. In our own experience, while the number of eggs in the feces of an infected patient varied considerably at different times, it was rare that no eggs could be found in examining 10 cover-glass preparations of the feces of a patient who had previously been found infected; there seems little doubt, therefore, that a more practical index of the amount of infection with intestinal worms in a community will be obtained by making a single examination of as many people as possible by the above method (10 preparations) than by making two examinations at different times of one-half as many people or three examinations of one-third as many people.

The technique of the microscopic examinations was simply to add to a very small amount of feces a drop or two of water on a 2 by 3-inch glass slide, cover it with a three-fourths inch square cover glass, and examine with a moderate power lens, either an 8 mm. or a one-third inch objective being sufficiently strong for a person familiar with the appearances of the various ova. Very fluid stools need no dilution. We found that diluting the feces, and thus obtaining a uniform,

transparent preparation which could be examined throughout the area of the cover glass was more satisfactory than the method advocated in the report of the Anæmia Commission in Porto Rico of simply compressing the undiluted feces by pressure upon the center of the cover glass, and thus obtaining a clear center for examination, but thick, opaque borders.

PRELIMINARY REPORT.—In May, 1903, a report was published upon the results obtained up to that date. (A statistical study of the intestinal parasites of 500 white male patients at the United States Hospital for the Insane. By Philip E. Garrison, Brayton H. Ransom, and Earl C. Stevenson. Bull. 13, Hyg. Lab., U. S. Pub. Health and Mar. Hosp. Serv., Wash., pp. 1-13.) These 500 cases are incorporated in the present paper, which is, therefore, a full report of all cases examined during the two years of the investigation.

ACKNOWLEDGMENTS.—It is a pleasure to acknowledge the courtesy and cooperation of those in charge of the institutions upon which we have been dependent for material for our work. To Doctors Richardson, White, and Stack, at the Government Hospital, and to Dr. Henry S. Noble, superintendent, and Dr. A. R. Diefendorf, pathologist, at the Connecticut Hospital, and also to the other members of the hospital staffs we are indebted for their interest in furnishing every facility for obtaining the specimens. It is only justice to mention in this connection the many nurses and attendants upon whom fell a large portion of what in some respects was the most difficult and most unpleasant part of the work.

FREQUENCY OF INFECTION.

Of the 3,457 persons examined, 349 were infected with intestinal worms, an average of 10.1 per cent. The parasites present were whipworms (*Trichuris trichiura*), pinworms (*Oxyuris vermicularis*), eelworms (*Ascaris lumbricoides*), hookworms (*Uncinaria* (*Necator*) *americana* and *Agchylostoma duodenale*^a), Cochin-China worms (*Strongyloides stercoralis*), the dwarf tapeworm (*Hymenolepis nana*), and the fat tapeworm (*Tænia saginata*).

CONCURRENT INFECTIONS.—The presence of two or more species of parasites in one person was found 36 times among our cases, the different forms occurring together as follows: *Trichuris* and *Ascaris*, 4 times; *Trichuris* and *Oxyuris*, 6 times; *Trichuris* and hookworms, 15 times; *Trichuris* and *Hymenolepis*, 5 times; *Trichuris* and *Strongyloides*, once; *Trichuris* and *Tænia saginata*, once; *Oxyuris* and *Ascaris*,

^a In the one case of hookworm disease in which we obtained the worms (autopsy) the parasite was *U. (N.) americana* [*Necator americanus*], and the large size of the eggs found in the other cases indicated that they also were infections with the American species. Most of the infections, however, were in men recently returned from the Philippine Islands, where the old world form (*A. duodenale*) is supposed to be common. In view of the possible uncertainty as to the species present in all but the one case we use the general term hookworm throughout for these infections.

once; *Oxyuris* and *Hymenolepis*, once; hookworms and *Strongyloides*, once; *Trichuris*, hookworms, and *Ascaris*, once. Thus, among the 349 infected persons there were 386 infections, an average of 11.17 infections for each 100 persons examined.

RELATIVE FREQUENCY OF THE DIFFERENT PARASITES.—The different species of worms were present in the following relative frequency:

	Infections.	Per cent.
<i>Trichuris trichiura</i>	266	7.69
<i>Oxyuris vermicularis</i>	45	1.30
Hookworms.....	36	1.04
<i>Ascaris lumbricoides</i>	17	0.49
<i>Hymenolepis nana</i>	12	0.35
<i>Strongyloides stercoralis</i>	8	0.23
<i>Tænia saginata</i>	2	0.06

Over two-thirds of the total number of infections were with the whipworm (*Trichuris trichiura*), while the eelworm (*Ascaris lumbricoides*), which is frequently stated to be the most prevalent intestinal worm of man and which presents about the same frequency as whipworms in other investigations (see p. 65), occurred only 17 times, namely, in about 0.5 per cent of the persons examined. As indicated in the introduction, the figures for the pinworm (*Oxyuris*) (1.30 per cent) in all probability do not fully represent the true frequency of that worm. *Tænia saginata* has been said to occur in about 1 per cent of the population, this opinion being expressed upon certain results of foreign investigators and its occurrence in the practice of physicians. Our much lower rate of 0.06 per cent would seem to indicate either that the prevalence of this parasite in the United States has been overestimated or that it is decreasing in frequency as a result of meat inspection, cold storage, etc. As will be shown, the infections with hookworms occurred for the most part among soldiers who had returned from service in the Philippine Islands. Perhaps the most striking result of our work is the finding of 12 cases of infection with the dwarf tapeworm (*Hymenolepis nana*). Only about 121 cases of infection with this cestode have been reported for man; about 27 of these (including our 12 cases and the cases found by Stiles in the Southern States in 1902) occurred in the United States. As Stiles has claimed in an earlier paper, there is strong indication that the dwarf tapeworm is the most common tapeworm in man in certain parts of this country.^a

^a As an addition to the North American cases of infection with this worm thus far recorded we can now add a case in Statesville, N. C., diagnosed upon microscopic examination of feces sent to us by Dr. H. F. Long, August, 1895.

RACE.

Whites and negroes were represented among our cases. The 123 children examined at the orphanage were of white race, and in the absence of children among the negroes examined it is obviously better to exclude the white children in order that the whites and negroes compared with regard to the relative frequency of helminthiasis among them may correspond in age.

The relative frequency of intestinal worms among whites and negroes in the total 3,334 adult cases examined was as follows:

	Examined.	Infections.	Per 100 persons.
White patients.....	2,875	303	10.54
Negro patients.....	459	57	12.42

A truer comparison between the two races may be made, however, if instead of comparing all whites and all negroes among our cases we select from each race patients who correspond in other conditions and make the comparison between two groups alike in all respects excepting race.

The negroes were all inmates of the Government Hospital, and 378 of the 459 had been residents of the District of Columbia prior to their admission. Selecting from the white patients at the Government Hospital those who were admitted from the District of Columbia, we obtain a group of 746 whites at the same institution admitted from the same limited locality, showing about the same range of age, duration of institutional life, and proportion of males and females as the 378 negroes. Following are the statistics for whites and negroes obtained from these restricted groups:

	Examined.	Infections.	Per 100 persons.
White patients.....	746	37	^a 4.96
Negro patients.....	378	47	^a 12.43

^a It may be noted that these 378 selected cases gave practically the same rate of infection (12.43 infections per 100 persons) as did the 459 negroes examined (12.42 infections per 100 persons). Among the whites, however, the percentage of infection among the patients admitted to the Government Hospital from the District of Columbia (4.96 infections per 100 persons) is remarkably lower than that for all whites examined (10.54 infections per 100 persons). This is due in part to the exclusion of the Connecticut cases (see p. 19 et seq.), but in a greater measure to the exclusion of patients admitted to the Government Hospital with a history of recent military or tropical life (see p. 49 et seq.).

It is seen that the rate of total infection among the negroes was between 7 and 8 per cent in excess of that found among the whites.

This greater frequency of intestinal worms among negroes than among whites held for both males and females in the above groups, as follows:

	Examined.	Infections.	Per 100 persons.
Male patients:			
Whites.....	397	22	5.54
Negroes.....	179	28	15.64
Female patients:			
Whites.....	349	15	4.30
Negroes.....	199	19	9.55

The relative frequency of each species of intestinal worm in whites and in negroes was as follows:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura</i> :			
White patients.....	746	28	3.75
Negro patients.....	378	37	9.79
<i>Oxyuris vermicularis</i> :			
White patients.....	746	4	0.54
Negro patients.....	378	1	0.26
Hookworms:			
White patients.....	746	2	0.27
Negro patients.....	378	3	0.79
<i>Ascaris lumbricoides</i> :			
White patients.....	746	0	0.00
Negro patients.....	378	3	0.79
<i>Strongyloides stercoralis</i> :			
White patients.....	746	3	0.40
Negro patients.....	378	0	0.00
<i>Hymenolepis nana</i> :			
White patients.....	746	0	0.00
Negro patients.....	378	3	0.79
<i>Tænia saginata</i> :			
White patients.....	746	0	0.00
Negro patients.....	378	0	0.00

Thus a higher rate of infection among negroes than among whites was found in the case of whipworms, of hookworms, of eelworms, and of dwarf tapeworms, the last two parasites having presented no infections among the white patients used in comparison. Pinworms and Cochin China worms gave higher percentages of infection among whites. Cochin China worms did not appear among the negroes in the above group.

The above results would seem to indicate that helminthiasis in general is more common among negroes than among whites; that whipworm infections are much more common among negroes; that negroes

are predisposed^a to infection with eelworms and dwarf tapeworms and (in a lesser degree) with hookworms; that pinworms and Cochin China worms are slightly more common among whites than among negroes.

The indication of a predisposition^a on the part of negroes to infection with *Hymenolepis nana* is much strengthened by certain figures not brought out above, namely, that among the 2,129 adult white patients excluded from the above group by selecting patients admitted to the Government Hospital from the District of Columbia, there appeared only 1 infection with the dwarf tapeworm (0.05 infection per 100 persons), while among the 81 adult negroes so excluded this parasite gave 2 infections (2.47 infections per 100 persons). The 123 children (white) examined at the orphanage, however, gave 4.88 per cent of infections with dwarf tapeworms, a rate considerably higher than that among adult negroes. This would seem to indicate simply that age is a more potent factor than race in determining the prevalence of this worm. (For age in its relation to helminthiasis, see pp. 23, 30.)

As stated in the introduction (p. 10), too much absolute importance must not be attached to the statistics for pinworms. As the contraction and transmission of infections with this parasite are largely questions of personal cleanliness, we might expect the actual relative prevalence of pinworm infections in the two races to be directly opposite to that indicated in our results.

With regard to the relative prevalence of hookworms among whites and among negroes in America, Stiles, in his report upon the prevalence of hookworm disease in the Southern States (1903, 51-52), says that clinically he found the malady comparatively rare in the negro race, and he raised the question whether this may be due, as suggested by Zinn and Jacoby (1896, 13), not to a lower frequency of infection among negroes, but to the negroes being less susceptible to the effects of the poison produced by the worms. This observation and the explanation suggested are strikingly confirmed by certain data contained in the latest publication (1906, Jan. 1, 10-11) of the anemia commission in Porto Rico. Of 14,560 white patients who appeared at the clinics for uncinariasis, 72+ per cent presented types of the disease classified clinically either as medium, intense, or very intense cases, leaving only 27+ per cent of light and very light cases. Of 670 negro patients, however, only 41+ per cent presented the severer types of the disease, while 58+ per cent were classified as light or very light cases. On the other hand, considering the severity

^a By racial predisposition to helminthiasis on the part of negroes we do not mean to imply any special physiological susceptibility to infection with intestinal worms such as is supposed to be present in the negro with regard to smallpox. While such a physiological susceptibility is not at present excluded, it is highly probable that a predisposition to intestinal worms in negroes would consist largely in a greater exposure to infection, depending on personal habits, environment, etc. —

of an infection as measured, not by the clinical symptoms, but by the number of worms present in the intestine (as indicated by the number of ova in the feces), the negroes were as severely infected as the whites; 78+ per cent of 13,219 white patients showed a great many, many, or a moderate number of hookworm ova in the feces; 21+ per cent showed few or very few ova. Of 673 negro patients, 76+ per cent showed a great many, many, or a moderate number of hookworm ova in the feces; 23+ per cent showed few or very few ova. These data, while showing conclusively that uncinariasis is a severer disease in whites than in negroes, do not indicate that there is any greater predisposition on the part of whites to hookworm infection and strengthen rather than weaken the conclusion indicated in our own results, namely, that hookworm infections are possibly more common among negroes than among whites.

SEX.

Among the whole number of persons examined (3,457), females were more frequently infected than males, as follows:

	Examined.	Infections.	Per 100 persons.
Males.....	2,311	247	10.68
Females.....	1,146	139	12.13

Considering each species of parasite separately, a higher rate of infection was present among female patients in the case of whipworms, of eelworms, and of the fat tapeworm; the other worms presented a higher percentage of infection among male patients:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura</i> :			
Males.....	2,311	149	6.45
Females.....	1,146	117	10.21
<i>Oxyuris vermicularis</i> :			
Males.....	2,311	38	1.64
Females.....	1,146	7	0.61
Hookworms:			
Males.....	2,311	33	1.43
Females.....	1,146	3	0.26
<i>Ascaris lumbricoides</i> :			
Males.....	2,311	8	0.35
Females.....	1,146	9	0.79
<i>Strongyloides stercoralis</i> :			
Males.....	2,311	7	0.30
Females.....	1,146	1	0.09
<i>Hymenolepis nana</i> :			
Males.....	2,311	11	0.48
Females.....	1,146	1	0.09
<i>Tænia saginata</i> :			
Males.....	2,311	1	0.04
Females.....	1,146	1	0.09

From the above it is seen that the higher rate of total infection found among female patients was due almost wholly to the higher percentage of whipworm infections which they presented.

While a higher rate of total infection was found among females than among males for the whole 3,457 persons examined, excessive helminthiasis in the females was not present at the Government hospital nor at the orphanage, but was confined entirely to the patients examined at the Connecticut hospital.

Among the 2,324 patients examined at the Government hospital the frequency of infection in males and in females was as follows:

	Examined.	Infections.	Per 100 persons.
Males.....	1,737	186	10.71
Females.....	587	39	6.64

This greater frequency of intestinal worms among men than among women at St. Elizabeth holds for both whites and negroes:

	Examined.	Infections.	Per 100 persons.
Whites:			
Males.....	1,494	150	10.04
Females.....	371	18	4.85
Negroes:			
Males.....	243	36	14.81
Females.....	216	21	9.72

If we select the patients admitted to the Government hospital from the District of Columbia, thereby restricting our cases to civilians and eliminating certain males who presented a high degree of helminthiasis apparently due to a history of military or of tropical life (see p. 49) we find the male rate of total infection still slightly in excess of the female rate:

	Examined.	Infections.	Per 100 persons.
Males.....	576	50	8.68
Females.....	548	34	6.20

Ascaris lumbricoides is the only parasite found at the Government hospital which gave a higher percentage of infection among females in that institution, as appears from the following.

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura</i> :			
Males.....	1,737	122	7.02
Females.....	587	30	5.11
<i>Oxyuris vermicularis</i> :			
Males.....	1,737	15	0.86
Females.....	587	3	0.51
Hookworms:			
Males.....	1,737	32	1.84
Females.....	587	1	0.17
<i>Ascaris lumbricoides</i> :			
Males.....	1,737	6	0.34
Females.....	587	3	0.51
<i>Strongyloides stercoralis</i> :			
Males.....	1,737	5	0.29
Females.....	587	1	0.17
<i>Hymenolepis nana</i> :			
Males.....	1,737	5	0.29
Females.....	587	1	0.17
<i>Tænia saginata</i> :			
Males.....	1,737	1	0.06
Females.....	587	0	0.00

At the orphanage, the higher rate of total infection which was found among males than among females was due entirely to one parasite—the dwarf tapeworm. Every other species present gave a higher percentage of frequency among the females. The statistics for the orphanage are as follows:

	Examined.	Infections.	Per 100 persons.
Total infections:			
Males.....	72	16	22.22
Females.....	51	10	19.61
<i>Trichuris trichiura</i> :			
Males.....	72	9	12.50
Females.....	51	7	13.73
<i>Oxyuris vermicularis</i> :			
Males.....	72	1	1.39
Females.....	51	1	1.96
Hookworms:			
Males.....	72	0	0.00
Females.....	51	1	1.96
<i>Ascaris lumbricoides</i> :			
Males.....	72	0	0.00
Females.....	51	1	1.96
<i>Strongyloides stercoralis</i> :			
Males.....	72	0	0.00
Females.....	51	0	0.00
<i>Hymenolepis nana</i> :			
Males.....	72	6	8.33
Females.....	51	0	0.00
<i>Tænia saginata</i> :			
Males.....	72	0	0.00
Females.....	51	0	0.00

Excluding *Hymenolepis nana*, the rates of infection in the two sexes with all other worms found were: Boys, 13.89 infections per 100; girls, 19.61 infections per 100.

Among the 1,010 patients examined at the Connecticut hospital, the frequency of intestinal worms among females was sufficiently greater than the frequency among males to overcome in the total results the higher rate of infection found among males both at the Government hospital and at the orphanage. The figures for the Connecticut hospital are as follows:

	Examined.	Infections.	Per 100 persons.
Total infections:			
Males.....	502	45	8.96
Females.....	508	90	17.72

Whipworms, eelworms, and the fat tapeworm gave a higher percentage of infection among Connecticut females than among Connecticut males; pinworms and Cochin China worms showed a higher rate among males than among females; hookworms were equally prevalent in the two sexes, and the dwarf tapeworm was not found among our Connecticut cases. The comparative statistics in question are as follows:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura</i> :			
Males.....	502	18	3.59
Females.....	508	80	15.75
<i>Oxyuris vermicularis</i> :			
Males.....	502	22	4.38
Females.....	508	3	0.59
Hookworms:			
Males.....	502	1	0.20
Females.....	508	1	0.20
<i>Ascaris lumbricoides</i> :			
Males.....	502	2	0.40
Females.....	508	5	0.98
<i>Strongyloides stercoralis</i> :			
Males.....	502	2	0.40
Females.....	508	0	0.00
<i>Hymenolepis nana</i> :			
Males.....	502	0	0.00
Females.....	508	0	0.00
<i>Tænia saginata</i> :			
Males.....	502	0	0.00
Females.....	508	1	0.20

It is evident that the higher rate of total infection in females than in males found in the Connecticut institution is almost wholly due to

the higher female rate of infection with whipworms, while pinworms gave a decidedly higher percentage among the male patients.

To draw a definite conclusion regarding the relative frequency of intestinal worms in males and in females from these seemingly contradictory results obtained from the different institutions is not unattended with difficulty, but there are certain considerations which will aid us considerably in arriving at a just interpretation of the figures above given.

With regard to the higher rate of infection found among males than among females at the Government hospital, it must be borne in mind that in that institution there were over 200 males with a history of recent military life, of whom 115 had seen service in the Philippine Islands and among whom there appeared a relatively high percentage of infection with whipworms and hookworms, while the females at the Government hospital, with the exception of a few criminal cases, had a history of civil life in the District of Columbia and may be considered, therefore, to present more nearly the average amount of helminthiasis in the normal population.

In explanation of the slightly higher rate of infection found among male civilians than among female civilians at the Government hospital, the suggestion may be offered that it might have been due indirectly to the influence of the soldiers admitted to the institution from the Army. It is not unnatural to suppose that the presence of the infections introduced by the soldiers among the male patients might be an additional source of infection to the civilians, civilians and soldiers being more or less intimately associated in their hospital life. The female patients would remain free from this influence. If this explanation is correct, it must follow that the higher male rate was due to a higher percentage of infection with those parasites which were exceptionally frequent among the soldiers, namely, whipworms and hookworms. In considering the relative frequency of each parasite in the two sexes at St. Elizabeth we have already seen that a higher rate of infection was present among the males in the case of whipworms and of hookworms, but also in the case of pinworms, of Cochin China worms, and of the dwarf tapeworm, parasites which did not show a particularly high percentage of infection among the soldiers; eelworms were more frequent among the female patients; the one infection with *Tænia saginata*, occurring among the males, could not be considered of significance with regard to the relative frequency of this parasite in the two sexes.

If now we consider separately the patients admitted to the Government hospital from civil life in the District of Columbia with regard to the relative frequency of each species of intestinal worm in males and in females, we shall find the results agreeing with those given

above for all patients at the Government hospital, namely, a higher rate of infection among males with whipworms, hookworms, pinworms, Cochin-China worms, and dwarf tapeworms, and a higher rate among females with eelworms, as follows:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura:</i>			
Males.....	576	36	6.25
Females.....	548	29	5.29
<i>Oxyuris vermicularis:</i>			
Males.....	576	3	0.52
Females.....	548	2	0.36
Hookworms:			
Males.....	576	5	0.87
Females.....	548	0	0.00
<i>Ascaris lumbricoides:</i>			
Males.....	576	1	0.17
Females.....	548	2	0.37
<i>Strongyloides stercoralis:</i>			
Males.....	576	2	0.35
Females.....	548	1	0.18
<i>Hymenolepis nana:</i>			
Males.....	576	3	0.52
Females.....	548	0	0.00
<i>Tænia saginata:</i>			
Males.....	576	0	0.00
Females.....	548	0	0.00

The greater frequency of intestinal worms among males than among females at the Government hospital, whether we consider the total number of patients in the institution or only those admitted from the District of Columbia, is evidently due, therefore, to a greater male infection with whipworms and hookworms, which is explainable by the excessive number of infections with these worms introduced among the males by the patients admitted from military and tropical life, and also to a greater male infection with pinworms, Cochin-China worms, and dwarf tapeworms, which is not so explainable.

These last three worms, however, were found to be more prevalent among males than among females at the other two institutions also, the dwarf tapeworm having been more frequent among males than among females at the orphanage, Cochin-China worms more frequent among males than among females at the Connecticut hospital, and pinworms more frequent among males than among females at both the orphanage and the Connecticut hospital.

On the whole, therefore, it would appear from our results that pinworms, Cochin-China worms, and dwarf tapeworms are more frequent parasites among males than among females. Eelworms and whipworms seem to be more common among females than among males,

since *Ascaris* gave uniformly a higher rate of infection among females and since *Trichuris* gave a higher rate among females at the Connecticut hospital and at the orphanage, while the higher male rate with whipworms at the Government hospital seems to be explained by infections introduced among the males by soldiers returned from recent army and tropical life. The hookworm infections found at the Government hospital, all but one of which occurred in males, may also be excluded from our sex statistics as being due to the influence of the army men; the three remaining hookworm infections, one at the orphanage and two at the Connecticut hospital, show a slightly higher rate per cent of infection among females than among males. Both males and females presented one infection with the fat tapeworm, the rate per cent being somewhat higher among females.

In interpreting these results as indications of the general relative frequency of each species of intestinal worm in the two sexes certain precautions are necessary. In the first place, the value of the statistics in this respect for any one species is directly proportional to the number of infections present. Thus the rates of infection with hookworms at the orphanage and the Connecticut hospital and the total rates for *Tænia saginata*, taken alone, have practically no significance with regard to the general relative frequency of these worms in the two sexes, since they represent only 2 and 3 infections, respectively. Cochin-China worms, with 8 infections and with a higher rate of infection among males than among females at both the Government and Connecticut hospitals, gave a much stronger indication of a relatively higher frequency in the male sex. In the case of *Hymenolepis nana* the evidence in favor of a greater frequency among males than among females seems fairly conclusive; 5 of the 6 infections with this worm found at the Government hospital and the 6 infections found at the orphanage were present in male patients. The greater frequency of the dwarf tapeworm among males than among females has been reported also by Cima in Italy.

Too much importance must not be attached to the excessive male infection with pinworms. Aside from the fact that a microscopic examination of the feces is not a satisfactory method of diagnosing pinworm infections, the simple life cycle of the worm and its direct transmissibility from person to person would indicate that it would spread in any part of an institution in which it happened to be introduced.^a

Ascaris lumbricoides, with a total of 17 infections and a higher rate of infection among females than among males in each of the three institutions, seems to show a predisposition to eelworm infection on

^a For the distribution of pinworms among the different sections and wards of the Connecticut hospital see page 53.

the part of females. If we accept the excessive infection with whipworms among males found at the Government hospital as due to infections introduced by the soldiers, the statistics obtained at the orphanage and at the Connecticut hospital would appear to establish a greater relative frequency of infection with this parasite among females than among males.^a

The significance of sex as a factor in the prevalence of intestinal worms, especially in rural districts, is further discussed on page 29 et seq.

AGE.

The results obtained from the first 500 cases examined (adult white males) seemed to show that the frequency of infection decreased as the age of the patients increased.^b This indication is strikingly strengthened in the total results obtained from our whole number of cases, including children and adults, whites and negroes, and males and females, but, as will be seen, it does not appear to hold for every class of patients.

In order to study the frequency of intestinal worms among persons of different ages, our patients were divided into four age groups, the divisions being such that each group would include those ages which might be supposed to agree most closely with respect to the conditions which would seem to be the most important factors in determining the degree of prevalence of helminthiasis (environment, habits, occupation, etc.). These groups, as arranged, are (1) persons under 15 years of age, (2) persons from 15 to 30 years old, (3) persons from 31 to 50 years old, and (4) persons 51 years of age or older.

The relative rate of total infection in the various groups for the whole number of persons examined^c was as follows:

	Examined.	Infections.	Per 100 persons.
Total infections:			
Under 15 years.....	123	26	21.14
15 to 30 years.....	572	90	15.73
31 to 50 years.....	1,341	153	11.41
Over 50 years.....	1,289	91	7.06

It is seen that there is a decided fall in the rate of infection in each group as we pass from the youngest to the oldest.

^a For the relative frequency of helminthiasis in males and females as reported by other authors see page 70.

^b See Garrison, Ranson & Stevenson, 1903, page 8.

^c Exclusive of 132 patients, whose ages could not be ascertained.

Following are the rates of infection in each age group with each species of parasite:

	Examined.	Infections.	Per 100 persons
<i>Trichuris trichiura:</i>			
Under 15 years.....	123	16	13.01
15 to 30 years.....	572	60	10.49
31 to 50 years.....	1,341	116	8.65
Over 50 years.....	1,289	60	4.65
<i>Oxyuris vermicularis:</i>			
Under 15 years.....	123	2	1.63
15 to 30 years.....	572	10	1.75
31 to 50 years.....	1,341	14	1.04
Over 50 years.....	1,289	17	1.32
Hookworms:			
Under 15 years.....	123	1	0.81
15 to 30 years.....	572	16	2.80
31 to 50 years.....	1,341	9	0.67
Over 50 years.....	1,289	3	0.23
<i>Ascaris lumbricoides:</i>			
Under 15 years.....	123	1	0.81
15 to 30 years.....	572	3	0.52
31 to 50 years.....	1,341	6	0.45
Over 50 years.....	1,289	4	0.31
<i>Strongyloides stercoralis:</i>			
Under 15 years.....	123	0	0.00
15 to 30 years.....	572	1	0.17
31 to 50 years.....	1,341	3	0.22
Over 50 years.....	1,289	4	0.31
<i>Hymenolepis nana:</i>			
Under 15 years.....	123	6	4.88
15 to 30 years.....	572	0	0.00
31 to 50 years.....	1,341	4	0.30
Over 50 years.....	1,289	2	0.16
<i>Tænia saginata:</i>			
Under 15 years.....	123	0	0.00
15 to 30 years.....	572	0	0.00
31 to 50 years.....	1,341	1	0.07
Over 50 years.....	1,289	1	0.08

The results for *Trichuris* and for *Ascaris* are in accord with the results for total helminthiasis in that the percentage of infection decreased with increasing age of the patients, the decrease being much more marked, however, in the case of whipworms than in that of eelworms. The frequency of pinworms showed little variation in the different age groups. The comparatively high frequency of hookworm infections in the second group (15 to 30 years) is perhaps explained by the large proportion of soldiers in that group who had returned from service in the Philippine Islands, over 12 per cent of whom were infected with this parasite. The figures for hookworms in the other three groups would seem to indicate a slight but consistent tendency to a decrease in frequency with increasing age of the patients. Cochin China worms, on the other hand, appeared to show some tendency to a

higher rate of infection among older persons. Dwarf tapeworms were decidedly more prevalent among the children (under 15 years) than in any group of adults.

Before attempting to draw any conclusions as to the general significance of the above results obtained from our total number of cases, we will consider what further information may be obtained by studying the relation between age and the prevalence of intestinal worms indicated by the results in the following classes of patients taken separately: Males and females, males and females at the Connecticut Hospital, white and negro males and females at the Government Hospital. Only in the first two classes (all males and all females) do we have the youngest age group (under 15 years) represented (by the orphanage children); the patients at the two hospitals all fell in the three older groups.

The total infections among males in the different age groups were as follows:

Years.	Examined.	Infections.	Per 100 persons.
Under 15.....	72	16	22.22
15 to 30.....	402	77	19.15
31 to 50.....	865	90	10.40
Over 50.....	876	43	4.91

Among the male patients, accordingly, as among males and females combined, the rate of infection decreased as we pass from the younger to the older age groups. With one exception, however, the rate of decrease is greater among males than among patients of both sexes, as appears from the following comparison:

Decrease in the rate of total infection:

	Infections per 100 persons.
From the first to the second age groups—	
Males and females.....	5.41
Males.....	3.07
From the second to the third age groups—	
Males and females.....	4.32
Males.....	8.75
From the third to the fourth age groups—	
Males and females.....	4.35
Males.....	5.49
From the first to the last age groups (total decrease)—	
Males and females.....	14.08
Males.....	17.32

It appears that the total decrease in the rate of infection from the first group (patients under 15 years) to the last group (patients over 50 years) is greater among males alone than among males and females together by over 3 infections per 100 persons; furthermore, that the decrease is greater among males alone than among males and females

together as we pass from the second to the third and from the third to the fourth age groups; as we pass from the first to the second group, however, there is a greater fall in the rate of infection in the case of males and females than in that of males.

Since we have found, therefore, that the decrease in the rate of infection with intestinal worms accompanying an increase in the age of the patients is considerably more marked in the results for males than in the results for males and females together, it must follow that this relation between age and helminthiasis is either absent or considerably less marked among the female patients examined. Before taking up the amount of infection at different ages among females, however, we may make a further study of the age statistics found among males by considering separately the white and the negro males at the Government Hospital and the male patients (white) at the Connecticut Hospital. The data in question are summarized in the following table:

Years.	Examined.	Infections.	Per 100 persons.
Total infections among white males at the Government hospital:			
15 to 30	238	45	18.91
31 to 50	516	60	11.63
Over 50	668	26	3.89
Total infections among negro males at the Government hospital:			
15 to 30	71	17	23.94
31 to 50	104	12	11.54
Over 50	56	7	12.50
Total infections among male patients (white) at the Connecticut hospital:			
15 to 30	93	15	16.13
31 to 50	245	18	7.35
Over 50	152	10	6.58

Among the white males at both hospitals the rate of infection decreased from the younger to the older age groups; the amount of the decrease was greater, however, among the males at the Government hospital than among those at Connecticut hospital. The negro males, on the other hand, while showing a more marked fall in the rate of infection than did the white males at either hospital as we pass from the second to the third age group, and a more marked total decrease than the Connecticut hospital males, presented a slightly higher percentage of infection among patients over 50 years old than among those between 31 and 50 years.

While it has not been thought desirable to enter into a consideration of the relative prevalence of each species of parasite at different ages among the male patients, since the number of infections with any one species in the various age groups would be rather small to give satisfactory results, it is worthy of note that while among both the white

and negro males at the Government hospital *Trichuris* is the predominating species in the statistics and the number of infections with *Oxyuris* is so small as to have little influence upon the total figures for all infections, among the males (white) at the Connecticut Hospital 22 of the total 45 infections which were present were with pinworms. Eliminating the pinworm infections, the results for the Connecticut males in the different age groups were as follows:

Years.	Examined.	Infections.	Per 100 persons.
15 to 30.....	93	6	6.45
31 to 50.....	245	12	4.90
Over 50.....	152	4	2.63

Among the total female patients (Washington and Connecticut) the rates of infection with all parasites in the different age groups were as follows:

Years.	Examined.	Infections.	Per 100 persons.
Under 15.....	51	10	19.61
15 to 30.....	170	13	7.65
31 to 50.....	476	63	13.23
Over 50.....	413	48	11.62

It is seen that among the females, as among the males, the youngest age group presented a considerably higher rate of infection than was found in any other group. As has been anticipated (p. 26), the progressive decrease in the rate of infection with advancing age is not present among the female patients as we have found it to be among male patients.

The frequency of infection at different ages in various classes of females was as follows:

Years.	Examined.	Infections.	Per 100 persons.
Total infections among white females at the Government Hospital:			
15 to 30.....	64	4	6.25
31 to 50.....	144	7	4.86
Over 50.....	148	6	4.05
Total infections among negro females at the Government Hospital:			
15 to 30.....	62	7	11.29
31 to 50.....	85	5	5.88
Over 50.....	52	7	13.46
Total infections among female patients (white) at the Connecticut Hospital:			
15 to 30.....	44	2	4.55
31 to 50.....	247	51	20.65
Over 50.....	213	35	16.43

Thus, the white females at the Government hospital showed a progressive decrease in the frequency of infection as we pass from the younger to the older age groups, though the decrease was less marked than that found among the white males.

The female negroes presented age statistics which differed radically from those of any other class of patients. The highest rate of infection occurred in the oldest group; a rate almost as high was present in the second age group (15 to 30 years); while the intermediate group (31 to 50 years) gave a percentage about half as high as either of the other two groups. It is noteworthy that among both male and female negroes the minimum rate of infection should have occurred among patients from 31 to 50 years of age, while in no class of white patients was the minimum rate found in this age group.

The irregularity with which the rate of infection varied in the different age groups among both male and female negroes and the lack of statistics for negroes under 15 years of age make it difficult to deduce from our results any conclusions with regard to the relative frequency of intestinal worms at different ages in the negro race; the indications are, however, that among negroes age is a less important factor in determining the prevalence of helminthiasis than it is among whites.

Among the females at the Connecticut hospital there appeared a much lower rate of infection among women from 15 to 30 years of age than among women above 30 years, those in the former group having given only 4.55 infections per 100, while the 460 women above 30 years old gave 86 infections, namely, 18.70 per 100 persons. Females over 50 years old, however, presented a lower frequency of infection than did the intermediate group (31 to 50 years).

It is evident that with exception of the negro patients the seeming difference between males and females regarding the relative frequency of intestinal worms at different ages is due to the results obtained from the women at the Connecticut hospital. As will be seen later, certain female wards at that institution presented an exceedingly high rate of infection with whipworms, for which no entirely satisfactory explanation could be discovered. The women upon these wards were more or less advanced in years, and the high rate of infection among them would naturally raise the rate for females of advanced age. Our figures for females of different ages seem to be abnormally influenced by the unexplained but very striking conditions strictly localized on these few wards; all other things being equal, females might be expected to show a relation between age and the prevalence of helminthiasis similar to that which appears among males.

It must be noted, however, that the women at the Connecticut hospital had been, in part, residents of rural districts and that certain conditions pertaining to the rural life of males and of females, dis-

cussed under the following heading, may have played a part in producing the difference which appears in our results between the prevalence of intestinal worms at different ages among males and among females.

SIGNIFICANCE OF SEX AND OF AGE AS FACTORS IN THE PREVALENCE OF INTESTINAL WORMS.

SEX.—It may be pointed out that the present statistics are governed chiefly by whipworms, namely, by a parasite which does not require an intermediate host, but a worm which is spread by means of the feces. Were we dealing with infections for which an intermediate host is necessary, as, for instance, liver fluke disease caused by *Opisthorchis sinensis*, lung fluke disease caused by *Paragonimus westermanii*, or infection with *Tænia saginata*, contracted by eating beef, the statistics would be influenced by the relatively greater intimacy between either sex and the source of infection. This same general principle ought to obtain in reference to parasites spread by eggs in the feces, but not requiring an intermediate host.

In localities, such as rural districts, not provided with a sewage system, there is naturally as a rule a greater amount of human fecal matter to the square meter within a radius of 50 meters of a dwelling than there is in the fields. In average daily life females would in general be more closely confined to the area surrounding the house than would males. Accordingly, the natural inference would seem to be that all other things being equal, under conditions as above stated, females should show a greater infection with parasites, as hookworms and whipworms, which are spread by means of the feces without intermediate host, than would males.

In the case of mining districts and excavations, more particularly if the houses are provided with properly kept privies, or in other districts where the fecal matter around the house is properly disposed of, the conditions would naturally be different and we should not expect to find this same relation between the amounts of infection in the two sexes.

Thus it is seen that the relative frequency of helminthiasis among males and females may vary according to the species of parasite with which we are dealing, and even with one and the same species, the frequency may vary according to the environment; in particular, according to the relative intimacy of the sex in question with the greater concentration of infectious material.

Stating this proposition in another way, it may be said that, while the existence of a physiological predisposition on the part of females can not at present be absolutely excluded, the relative frequency of a given parasite, or of helminthiasis in general, among males and females is apparently not so much a question of physiological predis-

position of the sex toward the parasite as it is a question of the relative intimacy existing between the average daily life of the sex and the more concentrated infectious material.

Thus, also, the difference in frequency of parasitism observed in the Connecticut and the St. Elizabeth women may be explained, at least in part, by the fact that the Connecticut female patients appear to have been recruited more from rural life, while the St. Elizabeth female patients appear to have been recruited almost entirely from city life.

In connection with hookworm disease in Porto Rico, Ashford, King, and Gutierrez (1904, 54) state that of 5,490 hookworm patients, 3,259 were males and 2,231, or 40.6 per cent, were females. This difference they interpret as largely due to chances offered for infection, "males naturally being more exposed from the nature of their occupation."

This conclusion is not quite so evident to us. In connection with this interesting question they bring out the fact (p. 49) that the laborers on coffee estates are doubly exposed to infection, namely, in that the environment of their dwellings is loaded with hookworm larvæ and in that a similar condition exists at their place of work. It may be pointed out that the infection around the houses would as a rule naturally be the severer; now it is, in general, the women and children who are subjected more to this concentrated infection than are the males; hence, other things being equal, it is among the females that the heavier infection would be expected. The question naturally arises, therefore, whether there is not some explanation other than occupation which would account for the higher number of male patients reported for Porto Rico. One such possibility occurs to us, namely, as stated by our colleagues, their patients came to the clinics, and many of them were obliged to walk miles in order to reach the place of treatment; their sex statistics therefore represent the number of males and females who visited the clinic and not the proportion of infected to noninfected males and females in the island, and the question would naturally arise whether males would not be more likely to visit the clinic than would the females, and whether the statistics would not have been reversed had they been based upon observations made at the homes instead of at the clinics. This possible interpretation is strengthened rather than weakened by the statement that "the degree of anæmia is less in females than in males, obeying to a certain extent, at least, the number of parasites with which each sex is infected," a statement which naturally gives rise to the thought that the severer female cases possibly failed to visit the clinic. A final point is that the sex statistics as reported are actual numbers and not the percentages of the infected to the uninfected; hence they do not represent the relative tendency of the two sexes to infection.

AGE.—In interpreting age as a factor in parasitism the conditions would appear theoretically even more complicated. Several authors

have shown that it is easier to infect younger animals with certain species of parasites than it is to infect older animals. In these cases an actual physiological predisposition is assumed, and it is apparently not illogical to assume a greater physiological difference between a child of 10 and an adult of 50 than between a male of 50 and a female of 50. Accordingly, in the case of children, it would appear that we have to deal not only with a question of the relative intimacy existing between the person and the infectious material, but also (at least in case of some species of parasites) with a physiological predisposition, due to the more susceptible condition of the tissues in younger hosts.

That the total columns should therefore show the highest percentage of infection under 15 years of age in both males and females is a fact due apparently both to physiology and to environment. But it is perfectly conceivable that environment (as in the case of miners, or of the soldiers from the Philippines, or in rural localities presenting special conditions) may play a much more important rôle than that played by physiological predisposition.

As the individual grows older this element of physiological predisposition would become progressively less and that of environment greater in importance, so that in persons over 15 years of age the prevalence of intestinal worms among persons of different ages, as also among the two sexes, would appear to be governed more by the degree of intimacy between persons of a given age and the source of infection and less by physiological conditions pertaining to that age. In other words, the difference in physiological predisposition between persons under 15 years of age and any older age group would be greater than this difference between any two older groups; hence it would play a smaller part as a factor in determining the prevalence of intestinal worms among the older groups.

It would appear that the intimacy between persons of different ages (above 15 years) and the concentrated infection found in the immediate vicinity of the dwelling in rural districts would not be the same in the two sexes. Up to about 15 years of age both males and females would be in close contact with this highly infected soil about the house, the girls naturally being somewhat more closely confined to this area than the boys. After 15 years of age, however, which is probably about the average age at which school life is ended in rural districts, the females would, as they became more and more confined to domestic duties with advancing years, likewise become more and more confined to the area of most concentrated infection about the dwelling; this would be true, at least until they reached such advanced age as would preclude their doing any work outdoors and restrict their work pretty closely to the house itself. The males, however, upon the ending of school days, would go to work in the fields and come less in contact with the immediate environment of the

dwelling than they had heretofore; passing middle life their work would become less laborious and bring them less in actual contact with the soil, but it still would take them away from the vicinity of the buildings.

In view of the above facts we should expect that in rural districts males over 15 years old would tend to show a decrease in the amount of helminthiasis as age increased, while females above that age might be expected to show an increase in the number of their infections, at least up to such advanced age as would cause them to give up the work about the yard and garden, so frequently done by women on farms and in small towns, and confine themselves strictly to indoor duties. As above stated, both males and females would give their highest rates of infection among those under 15 years of age, owing to the conditions both of environment and of physiological predisposition.

The only cases examined by us which gave a history of rural life under normal conditions are a part of those admitted to the Connecticut hospital. It was impossible, from obtainable data, to strictly separate among these cases all those having histories of rural and of urban life, but, as shown elsewhere (see p. 48), the great majority of infections occurred among the former class. It is notable, therefore, that in the Connecticut cases, among whom appeared residents of country districts, the rate of infection among males in the different age groups progressively decreased from the youngest (15 to 30) to the oldest (over 50 years), while among the females the rate of infection increased with advancing age from the second group (15 to 30 years of age) to the third group (31-50 years of age) and fell slightly in the last group (above 50 years).

If we had statistics for persons of rural life in Connecticut under 15 years of age, we should, accordingly, expect them to show, for both males and females, a still higher rate of infection than appears in any of the above groups.

Among the white patients at the Government hospital, none of whom presented a clear history of normal rural life, the rate of infection among both males and females shows a tendency to decrease with advancing age.

In connection with the very interesting age statistics given by Ashford, King, and Gutierrez (1904, 53) for hookworm diseases in Porto Rico, it may be pointed out that their figures refer to the proportion of their patients at given ages and not the proportion of the infected to the noninfected of any given age on the island. Thus, when they report only 35 cases for children under 5 years and 1,027 cases for the ages 10 to 14 years, this should not be interpreted as meaning that a person between 10 and 14 years is 29.9 times as liable to infection as a child under 5 years, but rather that a child of less than 5 years is not so likely to visit the clinic as is one of 10 to 14 years.

In other words, the liability to infection as expressed in the percentage of infected to the uninfected or to the whole number of any age period as found under similar conditions, is a more exact index of the probability of helminthiasis than is the number of cases treated for any given age. Still, for age periods between 10 and about 60 years the statistics give a more exact indication of conditions than for age periods below 10 and over 60 years, since for the persons of middle age there is not the same difficulty attendant upon visiting the clinic as there is for the very young and the very old.

When now it is considered that normally there is necessarily in any large area a greater number of children under 5 years of age than in any other 5-year period, also that women are more confined by the care of children under 5 years than of older children, and, further, that only 35 hookworm children under 5 years are given in the report as against 1,027 from 10 to 14 years, an additional argument is presented for suspecting that the sex and age statistics given for Porto Rico are governed by other factors beside the relative liability to infection presented by the two sexes or different ages.

LENGTH OF INSTITUTIONAL LIFE.

In considering the influence of institutional life upon the frequency of intestinal worms, we are confined to the patients examined at the two hospitals for the insane, since the necessary data were not obtained for the children at the orphanage.

The results of our first 500 examinations seemed to indicate that the frequency of infection with intestinal worms tended to decrease as the duration of institutional life lengthened. The statistics obtained from our whole number of adult cases (3,334) modify these earlier indications in a rather complicated manner.

Separating the patients examined according to their length of residence in the hospitals, we have made five groups, namely, (1) patients with a residence of less than 1 year; (2) from 1 to 3 years; (3) from 4 to 8 years; (4) from 9 to 15 years, and (5) of over 15 years.

The rates of infection with all parasites in these various groups of patients, including all adult cases examined,^a were as follows:

	Examined.	Infections.	Per 100 persons.
Total infections:			
Under 1 year.....	626	78	12.46
1 to 3 years.....	858	93	10.84
4 to 8 years.....	737	54	7.33
9 to 15 years.....	445	43	9.66
Over 15 years.....	585	76	12.99

^a Exclusive of 83 patients whose length of residence in the hospital could not be ascertained.

From the above figures it is seen that the lowest percentage of infection was present in the group of patients who had been in the hospital from 4 to 8 years. The first group (less than 1 year's residence) and the last group (over 15 years' residence) gave the highest and very similar rates of infection, each being between 12 and 13 infections per 100 persons. The frequency of infection in the second (1 to 3 years' residence) and in the fourth (9 to 15 years' residence) groups differed each from the other by only about 1 infection per 100 persons and each of these groups presented a rate of infection intermediate between the first and third groups and the third and fifth groups, respectively. In other words, there was a progressive decrease in the rate of infection from the first, through the second, to the third group of patients; then a progressive increase from the third group, through the fourth, to the last group containing patients of longest hospital residence; the rates of infection in the first and last groups agree very closely with each other; a similar agreement is seen between the second and fourth groups.

These results would seem to indicate that the frequency of intestinal worms tends to decrease for a certain period of institutional life (6 or 7 years) and then to increase when residence in the institution is prolonged beyond that length of time. Before attempting an interpretation of our results under this heading, however, we will proceed to examine further our statistics concerning the prevalence of helminthiasis at different periods of hospital life by considering the frequency of each species of parasite in each of the above groups, and also by studying the results obtained among various classes of our patients.

Following are the rates of infection at different periods of institutional life with each species of parasite represented:

	Examined.	Infections.	Per 100 persons
<i>Trichuris trichiura</i> :			
Under 1 year.....	626	58	9.27
1 to 3 years.....	858	66	7.69
4 to 8 years.....	737	32	4.34
9 to 15 years.....	445	29	6.52
Over 15 years.....	585	55	9.91
<i>Oxyuris vermicularis</i> :			
Under 1 year.....	626	1	0.16
1 to 3 years.....	858	8	0.93
4 to 8 years.....	737	9	1.22
9 to 15 years.....	445	11	2.47
Over 15 years.....	585	13	2.22
Hookworms:			
Under 1 year.....	626	13	2.08
1 to 3 years.....	858	12	1.40
4 to 8 years.....	737	5	0.68
9 to 15 years.....	445	1	0.22
Over 15 years.....	585	0	0.00

	Examined.	Infections.	Per 100 persons.
<i>Ascaris lumbricoides:</i>			
Under 1 year.....	626	6	0.96
1 to 3 years.....	858	2	0.23
4 to 8 years.....	737	4	0.54
9 to 15 years.....	445	0	0.00
Over 15 years.....	585	1	0.17
<i>Strongyloides stercoralis:</i>			
Under 1 year.....	626	0	0.00
1 to 3 years.....	858	3	0.35
4 to 8 years.....	737	1	0.14
9 to 15 years.....	445	0	0.00
Over 15 years.....	585	4	0.68
<i>Hymenolepis nana:</i>			
Under 1 year.....	626	0	0.00
1 to 3 years.....	858	1	0.12
4 to 8 years.....	737	3	0.41
9 to 15 years.....	445	1	0.22
Over 15 years.....	585	0	0.00
<i>Tænia saginata:</i>			
Under 1 year.....	626	0	0.00
1 to 3 years.....	858	1	0.12
4 to 8 years.....	737	0	0.00
9 to 15 years.....	445	1	0.22
Over 15 years.....	585	0	0.00

The rate of infection with whipworms is thus seen to have varied in the different groups in practically the same manner as did the rate of total infection. Pinworms progressively increased in frequency with increasing length of institutional life, the only exception being the very slight excess of infection (0.25 infections per 100 persons) among patients of 9 to 15 years' hospital residence over the infection present among patients in the last group. The rate of infection with hookworms progressively decreased from over 2 infections per 100 persons in the first group to 0 infection in the last group. The eelworm showed a higher percentage of infection among persons of a comparatively short hospital residence, though its distribution among the different groups of patients was irregular. The irregular distribution and the small number of infections with Cochin China worms, with dwarf tapeworms, and with fat tapeworms make it impossible to detect any special relation between the prevalence of these parasites and the length of institutional life.

The combined effect of the infections with *Oxyuris* and hookworms would tend to make the rate of infection slightly higher among patients of a long and of a short institutional life than among patients of an intermediate length of hospital life, as follows:

Years.	Examined.	Infections.	Per 100 persons.
Under 1.....	626	14	2.24
1 to 3.....	858	20	2.33
4 to 8.....	737	14	1.90
9 to 15.....	445	12	2.70
Over 15.....	585	13	2.22

The number of infections with these two worms was too small, however, to account in any considerable degree for the similar variation in the frequency of total infections at different periods of hospital residence, the rates of total infection being governed largely by the relatively high number of infections with whipworms.

SIGNIFICANCE OF INSTITUTIONAL LIFE AS A FACTOR IN THE PREVALENCE OF INTESTINAL WORMS.

The peculiar result brought out above, namely, a decrease in the rate of infection for a certain length of institutional life and a subsequent increase, may be accounted for in a small measure by the combined rates of infection with *Oxyuris* and hookworms, but in a much greater degree by the *Trichuris* infections. We have not been able to explain this peculiar variation in a manner mathematically exact, but certain considerations, as set forth in the following paragraphs, offer at least a possible explanation.

Upon admission to the hospital, the patients would naturally have a given amount of infection, greater or less, according to the prevalence of intestinal worms under the conditions and among the population from which the patients came. These infections would, of themselves, tend to die out upon removal from the source of infection and in the absence of a new source resident within the hospital itself; this disappearance of the parasites would be more or less rapid according to the longevity of the worms, the amount of anthelmintic and purgative treatment to which the patients were subjected, and to the degree of resistance of the parasites to such treatment.

It may be assumed, however, that there is among the patients of every institution, as in the population at large, a given amount of endemic helminthiasis. Furthermore, it seems probable that in a long-established institution this amount of infection with intestinal worms would be fairly constant—that is, it would be the amount which the sanitary and other conditions in the institution will support and propagate.

In its last analysis the increase or decrease of intestinal helminthiasis among patients after admission to an institution and the rate of such increase or decrease are governed by the relation between the pertinacity with which infections present on admission cling to their hosts and the rapidity with which new infections are implanted from sources within the institution. For instance, if the infections present at the time of admission are very persistent and if the new sources of infection within the institution exert their influence promptly there would result a rise in the rate of infection. On the other hand, if the infections present at the time of admission disappeared quickly, before the sources of infection within the hospital had time to exert their influence by implanting new infections, the percentage of infection would fall. While the rate of infection might thus vary at different periods after admission, the general tendency would be toward one fixed rate, namely, the amount of infection in harmony with the conditions within the institution. In the case of patients entering the hospital with a relatively high frequency of intestinal worms there would eventually be a decrease in the percentage of infection among them; in the case of patients entering the hospital with a relatively low frequency of intestinal worms there would be eventually an increase in the rate.

This explanation applies, of course, only to those parasites which do tend to die out upon removal from the original source of infection, and not to those, such as *Oxyuris vermicularis*, in which the infected person is able, by direct and continual autoinfection, to continue his infection indefinitely. In the case of such a parasite not only would we not necessarily expect the infections admitted to the hospital to disappear (in the absence of treatment), but each case admitted would be a source of infection to other (uninfected) patients, so that the general tendency would be to an increase in the amount of infection as the institutional life of the patients lengthened.

With the exception of *Oxyuris vermicularis*, and possibly also of *Hymenolepis nana*, all of the parasites which appeared among our cases must in the course of their life cycle pass through certain evolutionary changes after leaving the original host before they become infectious, and the time and the conditions demanded for this evolution eliminate the possibility of direct autoinfection. In the absence of an external source of infection, therefore, these parasites naturally tend to disappear from the infected patients.

If, then, some patients may experience a decrease and other patients an increase in the amount of helminthiasis after admission to an institution, and, furthermore, if the rates of increase or decrease depend upon the relation between the longevity of an infection on the one hand and the implanting of new infections on the other, it follows that under certain conditions of initial rates of infection, rates of increase

and decrease, and of numerical proportion between the two classes of patients, we would find a lower rate of infection among all patients who had resided in the institution an intermediate length of time than among either all patients upon admission or all patients of longest residence.

That this may obtain is shown by the following hypothetical case: Let it be assumed that the endemic rate of infection within the institution is 15 per cent and that 100 patients enter the institution with 25 per cent of infection and 100 other patients enter with 5 per cent of infection. The average rate of infection for the 200 patients upon admission would be 15 per cent, namely, the same percentage present among patients who, by reason of long residence in the institution, conformed in the amount of their parasitism to the endemic rate of the institution. Under the influences of the two elements above noted, namely, (1) the dying out of the infections present at the time of admission, because of removal from the previous source of infection, and (2) the implanting of new infections from the sources within the institution, the infection among the 100 patients entering the hospital with 25 per cent of infection will gradually decrease until it reaches 15 per cent, the amount which the conditions within the institution will support and propagate. Under these same influences the infection among the 100 patients with 5 per cent of infection upon admission will gradually increase until it reaches the endemic rate, namely, 15 per cent.

Let us make the further assumption that the decrease in the amount of infection among the patients highly infected upon admission is such that at the end of five years their helminthiasis has fallen from 25 per cent to 12 per cent, and, on the other hand, that the infection among those with low helminthiasis upon admission has risen from 5 to 8 per cent. Expressed in actual figures instead of percentages, let it be assumed that in five years' time 20 of the 25 infected patients of the first class lose all of their parasites and that the same proportion (namely, 4 cases) of the second class lose all of their worms. We would then find 5 cases of the first and 1 case of the second class still showing original helminthiasis. The two classes would, however, be liable to the same number of new infections, say 7. This would give us 12 cases of infection in the first class and 8 cases in the second, a total of 20 infections (10 per cent).

The average rate of infection, then, for the 200 persons after five years' residence in the institution would be 10 per cent, namely, 5 per cent lower than that among the 200 patients upon admission and even 5 per cent lower than the rate endemic within the hospital itself.

It is possible to put this explanation to a rough test among our own cases. At the Government hospital we had a comparatively high frequency of intestinal worms among the incoming patients, due to

the great prevalence of parasites among the men admitted from the Army. Among the females at the Government hospital and among both males and females at the Connecticut hospital the frequency is comparatively low upon admission, these patients being admitted almost entirely from civil life.

In this connection we have prepared Table 1, showing the apparent influence of institutional life when the frequency of whipworms is high in newly admitted patients (army men and male negroes admitted to the Government hospital) and when it is low (Connecticut patients and women admitted to the Government hospital).

By considering *Trichuris* alone in this comparison we make the test not only simpler but more exact also, as the number of infections with the other worms (except *Oxyuris*) is too few to form satisfactory grounds for study in this relation.

Among the white and negro males at the Government hospital, the two classes showing the highest initial percentage of infection (12.67 and 13.79 per cent), the rate tends to decrease as the duration of institutional life of the patients advances.

Among the white women at St. Elizabeth's and both males and females at the Connecticut hospital, with a prevalence of 3, 3.23, and 8.70 per cent of infection upon admission, there appears to be a general tendency to an increase in the rate of infection among the patients of longer residence in the hospital.

In no case, however, is there a consistent variation in the rate of infection throughout all the groups. Among the negro women the figures vary so erratically that they do not seem to conform to any possible rule. Among the white males the rate, after consistently falling from 12.67 per cent in the first group of less than one year's residence to 1.61 per cent among the patients of from nine to fifteen years' residence, rises to 4.26 per cent in the last group (of those who had been in the hospital over fifteen years). The male negroes, after dropping from 13.79 in the first group to 10.17 in the second, maintain practically the same rate throughout the remaining groups until reaching the last (of over fifteen years of hospital life), where the infection drops to 5.88 per cent.

Among the classes of patients who come to the hospital with a relatively low degree of infection the white women at St. Elizabeth's present a uniformly increasing rate from 3 per cent, among those recently admitted, to 7.69 per cent among those admitted fifteen years or more prior to examination, with the exception that among the 66 women who had been in the hospital from four to eight years no infections appear. The Connecticut males show 3.23 per cent of infection upon admission, 4.38 per cent in the next group, of from one to three years' residence, 2.27 and 3.70 per cent, respectively, in the two succeeding groups, and reach 5.26 per cent, their highest rate, among those of

over fifteen years' residence in the hospital. The Connecticut women enter the hospital with 8.70 per cent of *Trichuris* infections; among those of from one to three years' residence the rate falls slightly to 7.75 per cent; thereafter there is a comparatively rapid rise until it reaches its maximum of 34.69 per cent among the patients of longest institutional life.

Notwithstanding the above inconsistencies in the variations in the percentage of infection in the different classes of patients among the groups of varying lengths of hospital life, the figures in the table do, we think, bring out the general tendencies above noted; these tendencies are more clearly apparent when we compare directly the rate of infection among the patients admitted to the hospital within one year prior to examination with that among the patients who had lived in the hospital over fifteen years, taking first those who show a high frequency of infection upon admission and then those who enter the hospital with a comparatively low frequency, as follows:

Comparatively high rate of infection on admission.

St. Elizabeth white males:	Per cent.
Less than one year's residence.....	12.72
More than fifteen years' residence.....	4.26
St. Elizabeth male negroes:	
Less than one year's residence.....	13.79
More than fifteen years' residence.....	5.88

Comparatively low rate of infection on admission.

St. Elizabeth white females:	
Less than one year's residence.....	3.00
More than fifteen years' residence.....	7.69
Connecticut males:	
Less than one year's residence.....	3.23
More than fifteen years' residence.....	5.26
Connecticut females:	
Less than one year's residence.....	8.70
More than fifteen years' residence.....	34.69

TABLE I.—*Influence of institutional life upon the prevalence of Trichuris trichiura among patients with different degrees of infection upon admission.*

	1 year.			1 to 3 years.			4 to 8 years.			9 to 15 years.			15 years.			(?)		
	Exam-ined.	Infec-tions.	Per cent.	Exam-ined.	Infec-tions.	Per cent.	Exam-ined.	Infec-tions.	Per cent.	Exam-ined.	Infec-tions.	Per cent.	Exam-ined.	Infec-tions.	Per cent.	Exam-ined.	Infec-tions.	Per cent.
Government Hospital:																		
White males.....	292	37	12.67	380	34	8.95	298	6	2.01	186	3	1.61	305	13	4.26	33	4	12.12
Negro males.....	58	8	13.79	59	6	10.17	58	6	10.34	28	3	10.71	34	2	5.88	6	0	0
White females.....	100	3	3.00	84	3	3.57	66	0	0	41	2	4.88	65	5	7.69	15	0	0
Negro females.....	68	4	5.88	46	6	13.04	36	1	2.78	24	4	16.67	26	1	3.85	16	1	6.25
Connecticut Hospital:																		
Males (white).....	62	2	3.23	160	7	4.38	132	3	2.27	81	3	3.70	57	3	5.26	10	0	0
Females (white).....	46	4	8.70	129	10	7.75	147	16	10.88	85	14	16.47	98	34	34.69	3	1	33.33
Total.....	626	58	9.27	858	66	7.69	737	32	4.34	445	29	6.52	585	58	9.91	83	6	7.23
More heavily infected.....	350	45	12.86	439	40	9.11	356	12	3.37	214	6	2.80	339	15	4.42	39	4	10.26
Less heavily infected.....	276	13	4.71	419	26	6.21	381	20	5.25	231	23	9.96	246	43	17.48	44	2	4.55
Less heavily infected (except negro women).....	208	9	4.33	373	20	5.36	345	19	5.51	207	19	9.18	220	42	19.09	28	1	3.57

It is rather striking that in the St. Elizabeth cases and among the Connecticut males the infection found among patients of more than fifteen years' residence varies (p. 40) only as follows: 4.26 per cent, 5.26 per cent, 5.88 per cent, and 7.69 per cent—figures which seem to indicate the approximate amount of endemic helminthiasis in the wards in question. It will further be noticed that at St. Elizabeth the final infection of the negroes (5.88 per cent) is higher than that of the white males either at St. Elizabeth (4.26 per cent) or at Connecticut (0.26 per cent). These statistics are in harmony with the general conclusion that the worms were more common among negroes than among whites. It will also be noticed that the St. Elizabeth white females presented a higher infection (7.69 per cent) than the white males at either St. Elizabeth (4.26 per cent) or Connecticut (5.26 per cent), statistics which are in harmony with the general conclusion that the worms in question are more common among females than among males.

The very high percentage (34.69 per cent) found among the Connecticut females is due to a certain few wards and to conditions which were not clear to us (see p. 58).

Taking a total of the cases (negro women excepted), it is found that of the classes showing heavy infection (12.86 per cent) within less than 1 year after entrance this infection has decreased in cases of 1 to 3 years (to 9.11 per cent); also in cases of 4 to 8 years (3.37 per cent) and 9 to 15 years (2.80 per cent); then it increased after 15 years to 4.42 per cent; classes showing a light infection (4.33 per cent) within 1 year after entrance have increased in 1 to 3 years to 5.36 per cent, in 4 to 8 years to 5.51 per cent, in 9 to 15 years to 9.18 per cent, and after 15 years to 19.09 per cent. Inserting the negro women in the last series, the statistics change slightly, as follows: 4.71 per cent, 6.21 per cent, 5.25 per cent, 9.96 per cent, 17.48 per cent.

The general tendencies indicated by the results set forth on pages 39-42 therefore give some plausible confirmation to the principle above stated, namely, that the influence of institutional life upon the prevalence of intestinal worms not directly transmissible from person to person is to lower or raise the rate of infection among newly admitted inmates until it reaches a certain fairly constant amount, which the conditions of life in the institution will support.

On this basis, then, the amount of infection found among patients of over 15 years of hospital life represents approximately the amount endemic within the hospital itself, and, with one exception, this amount is fairly uniform among all of the above classes of patients and in the two institutions; it certainly is so when compared with the wide difference in the prevalence of intestinal worms in the different classes upon admission. The one exception occurs in the Connecticut women, who upon admission show the intermediate rate of 8.70 per cent and after

15 years of hospital life the remarkably high frequency of 34.69 per cent. It is difficult to understand how in the same institution a rate of 34.69 per cent of infection should be present among women of over 15 years' residence, while the men of like length of residence should show only 5.26 per cent; or that the women of such long residence in one institution should give 34.69 per cent of infection, while the women of another institution, not essentially different in internal arrangement or external situation, should give only 7.69 per cent. This high percentage of infection which appears in certain classes of the Connecticut women throughout our study is due to the exceedingly great prevalence of *Trichuris trichiura* found upon and confined to three or four female wards at the Connecticut hospital, where the rate reaches as high as 40, 50, and in one ward 75 per cent. The amount of infection upon these few wards was phenomenal and not even approached by any other wards at the Connecticut institution or by any at the Government Hospital, excepting two wards which, among patients almost exclusively soldiers recently returned from the Philippine Islands, presented 44.12 and 46.48 per cent of infection.

It seems, therefore, that the high rate of 34.69 per cent of infections with the whipworm is by no means the rate normally present among women who have lived 15 years in the Connecticut hospital, but rather is an abnormally high rate due to conditions found upon a few heavily infected wards (see pp. 53-64).

It is evident that the apparent influence of institutional life as indicated in the total figures for all our cases, namely, a decrease in the amount of infection for about 6 or 7 years of institutional life and an increase thereafter, is but a result of combining patients who, entering the hospital with a high rate of infection, tend to gradually lose their parasites, and patients of whom comparatively few are infected upon admission and among whom the rate of infection tends to rise.

NATIVITY.

We were unable to obtain from the hospital records of the patients of foreign birth data relative to their length of residence in the United States. The nativity of the children at the orphanage was not ascertained, but the great majority was doubtless of American birth. Our comparison with regard to nativity is, therefore, simply between the native and foreign born among the adult patients examined.

There were 215 adults of whose birthplace there was no record. Among the remaining 3,119 patients the frequency of infection with all parasites varied in the native and the foreign born as follows:

	Examined.	Infections.	Per 100 persons.
Native born.....	2,096	204	9.73
Foreign born.....	1,023	117	11.44

This greater frequency of infection among the foreign born exists despite the fact that the native born included 396 negroes, among whom, as already shown, the rate of infection is particularly high. Among whites alone the statistics of total infection for native and foreign born were as follows:

	Examined.	Infections	Per 100 persons.
Native born.....	1,637	153	9.35
Foreign born.....	1,020	117	11.47

The frequency of infection with intestinal worms is seen, therefore, to be greater among foreign-born whites than among native-born whites by over 2 infections per 100 persons.

The various species of worms occurred in native and in foreign born whites as follows:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura:</i>			
Native born.....	1,637	104	6.35
Foreign born.....	1,020	87	8.53
<i>Oxyuris vermicularis:</i>			
Native born.....	1,637	23	1.41
Foreign born.....	1,020	14	1.37
Hookworms:			
Native born.....	1,637	14	0.86
Foreign born.....	1,020	8	0.78
<i>Ascaris lumbricoides:</i>			
Native born.....	1,637	3	0.18
Foreign born.....	1,020	7	0.69
<i>Strongyloides stercoralis:</i>			
Native born.....	1,637	8	0.49
Foreign born.....	1,020	0	0.00
<i>Hymenolepis nana:</i>			
Native born.....	1,637	0	0.00
Foreign born.....	1,020	0	0.00
<i>Tænia saginata:</i>			
Native born.....	1,637	1	0.06
Foreign born.....	1,020	1	0.10

From the above figures it is evident that the higher rate of total infection among persons of foreign nativity was due largely to the greater frequency of whipworm infections which they presented; eel-worm infections also gave a higher rate per cent among the foreign-born patients. Pinworms, on the other hand, presented a slightly greater frequency among patients of native birth, and the 8 infections with Cochin China worms all occurred among the native born.

The above indications of a greater frequency of intestinal worms among foreign than among native born patients were found, however, not to be equally present among all nationalities, and in the case of immigrants from one country the rate of total infection was somewhat less than among persons of native birth. The great majority of foreign-born patients were Irish, German, and English. Among the other nationalities represented—none, however, in sufficient numbers to be considered separately—Canadians, Swedes, Swiss, Austrians, Poles, and Italians largely predominated.

The rates of total infection among the patients of German, of English, of Irish, and of other foreign birth were as follows:

	Examined.	Infections.	Per 100 persons.
German born.....	258	19	7.36
English born.....	79	8	10.13
Irish born.....	424	58	13.68
Other foreign born.....	179	21	11.73

The lowest frequency of helminthiasis in foreign-born patients was present among those of German birth, the rate of total infection among the Germans being lower than that for native white Americans, and lower also than the rate reported by any author for Germans in their own country (see table, p. 65). Patients of English nativity gave a somewhat higher frequency of infection than did native Americans, but a lower rate than the average percentage of infection among all foreign-born persons examined. The high rate of infection among patients of Irish nativity exceeds even that found among American negroes and was evidently responsible, in the most part, for the greater frequency of intestinal worms among Americans of foreign than of native birth.

We were unable to discover in our statistics any evidence of a special predisposition on the part of one nationality to infection with any particular species of intestinal worm.

It is interesting to note the difference in the prevalence of helminthiasis between the two sexes in the three nativities most largely represented, namely, German, English, and Irish. From the following figures it will be seen that while among patients of German and of Irish birth the rate of total infection was about 9 infections per 100 persons higher among females than among males, among the English-born patients the reverse obtained, the males having given a rate of infection nearly 5 infections per 100 persons in excess of the rate present among females:

	Examined.	Infections.	Per 100 persons.
German born:			
Males.....	209	12	5.74
Females.....	49	7	14.29
Irish born:			
Males.....	263	27	10.27
Females.....	161	31	19.25
English born:			
Males.....	63	7	11.11
Females.....	16	1	6.25

It also appears from the above figures that if foreign-born males and females are considered separately, the patients of German, of English, and of Irish nativities do not maintain the same order as regards the frequency of helminthiasis in the two sexes. For males, the highest rate of infection was found among the English born, the next highest among the Irish born, and the lowest rate among the German born; for females, the highest rate of infection occurred among Irish-born patients, the next highest among Germans, and the lowest rate among the women of English nativity.

The greater frequency of intestinal worms among English-born males than among English-born females held even at the Connecticut hospital, where the rate of infection in general was considerably higher among the female patients. As will be seen, however, we are reduced to very small bases in making this comparison between males and females among the English-born patients at the Connecticut hospital, and the results would hardly be of interest except when taken in connection with the comparisons between the sexes among patients of foreign nativities given above:

	Examined.	Infections.	Per 100 persons.
Males.....	12	2	16.66
Females.....	10	1	10.00

HISTORY OF PATIENTS PRIOR TO ADMISSION TO THE HOSPITALS.

Our statistics under this head are confined to the patients at the United States Government and the Connecticut State hospitals, sufficient data not having been obtainable for the children at the orphanage to consider them in this connection.

PLACE OF RESIDENCE.—Our material is not well adapted for studying the variations in the prevalence of infection in different localities. It was desirable in the first place to eliminate as completely as possible the influence of institutional life, and this has been done by selecting

patients admitted to the hospitals within one year prior to the time of their examination. Such a selection gave a total, for both hospitals, of 626 persons. Of these 626 persons of comparatively short institutional life, 108 had been admitted to the Connecticut hospital from the State of Connecticut, 256 had been admitted to the Government hospital from the District of Columbia, and the remainder (262) had been received at the Government hospital either from other institutions or more or less directly from the widely scattered localities attendant upon service in the Army or Navy.^a About the only comparison possible to be made from our results, therefore, between different localities is one between Connecticut and the District of Columbia.

The rates of total infection among our patients who were residents either of Connecticut or of the District of Columbia were as follows, each group being restricted to patients who had been in the hospitals less than one year:

	Examined.	Infections.	Per 100 persons.
Connecticut.....	108	10	9.26
District of Columbia.....	256	21	8.20

Although the District of Columbia patients included both whites and negroes, they are seen to have presented a rate of total infection lower by about 1 infection per 100 persons than the rate found among the Connecticut patients, all of whom were whites. If, in order to draw a comparison between the white residents of the two localities in question, we eliminate the negroes from the District of Columbia patients, the following results are obtained:

	Examined.	Infections.	Per 100 persons.
Whites.....	148	8	5.41
Negroes.....	108	13	12.04

From these figures it would appear that while negroes from the District of Columbia presented a rate of infection considerably in excess of that found among patients admitted from Connecticut (whites), the latter gave nearly twice as many infections per 100 persons as did the white patients admitted from the District of Columbia.

Only 4 species of parasites were represented by infections in the different groups of patients above considered, namely, whipworms (25 infections), eelworms (4 infections), hookworms (1 infection), and

^a The soldiers who had served in the Philippines are considered under the head of military service rather than in this connection.

pinworms (1 infection). These infections were distributed among the different groups as follows:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura:</i>			
Connecticut.....	108	6	5.55
District of Columbia—			
Whites.....	148	7	4.73
Negroes.....	108	12	11.11
<i>Ascaris lumbricoides:</i>			
Connecticut.....	108	3	2.77
District of Columbia—			
Whites.....	148	0	0.00
Negroes.....	108	1	0.93
Hookworms:			
Connecticut.....	108	0	0.00
District of Columbia—			
Whites.....	148	1	0.68
Negroes.....	108	0	0.00
<i>Oxyuris vermicularis:</i>			
Connecticut.....	108	1	0.93
District of Columbia—			
Whites.....	148	0	0.00
Negroes.....	108	0	0.00

The rates of infection with whipworms are seen to vary in the different groups in the same manner as did the rates of total infection. Eelworms were more prevalent among the patients admitted from Connecticut than among the negroes from the District of Columbia.

The patients admitted from the District of Columbia were practically residents only of the city of Washington, while the Connecticut patients were received from both rural districts and cities, and in this fact probably lies the explanation of the higher rate of infection found among the Connecticut cases, rural life being naturally more favorable to the prevalence of intestinal worms than is city life.

Rural and city life.—Some confirmation of the above explanation of the greater prevalence of intestinal worms among the Connecticut than among the District of Columbia patients is found when we separate from the 108 Connecticut cases those admitted from the larger cities of the State. As the hospital records give simply the town from which the patients were received, and as the New England towns commonly include both rural and urban population, it is impossible to draw a well-defined line between the Connecticut patients admitted from country and from city life. By separating those admitted from the cities of Hartford, Bridgeport, and New Haven, however, cities which are coextensive with the towns of the same name, we are able to obtain a small group of patients with an assured history of city life. Twenty-six, or about one-fourth of the 108 Connecticut patients under consideration, fall within this group.

Among them, however, we find but one infection (*Trichuris*), or only one-tenth the number present among the whole 108 patients. In other words, while the 108 patients with histories of both rural and urban life gave 9.26 infections per 100, the 26 with a history of city life gave only 3.84 infections per 100.

This rate of infection among patients admitted to the Connecticut hospital from city life within one year prior to examination is considerably lower than that among the white patients admitted within the same period to the Government hospital from the city of Washington (5.41 per 100).

While the results obtained for city residents in Connecticut are based on only 26 patients, presenting but 1 infection, they are at least confirmatory of the view that intestinal parasites are less frequent among the urban than among the rural population in that State, and indicate further that the higher rate of infection present among patients admitted from Connecticut than among those admitted from the District of Columbia (Washington) is due to the fact that the latter were admitted almost wholly from city life while the Connecticut patients were in part residents of country districts.

OCCUPATION.—The male civilians are so equally distributed among so many different occupations that the statistics for any one group remain too small to permit of definite conclusions in regard to the relative prevalence of intestinal worms in the various trades, professions, etc., represented among our cases. There remain, however, the male patients at the Government hospital admitted from the military service of the United States. These men present a history of such a distinct and special nature that they are considered under a subheading.

Military service.—Besides soldiers admitted to the hospital directly from active service in the United States Army, we consider in this class of patients sailors received from the Navy and old soldiers from the National Soldiers' Homes. The soldiers received more or less immediately from active service fall naturally (from a parasitological viewpoint) into three groups, namely, those admitted before the Spanish-American war, hence from the Regular Army posts; those admitted during and after the war, hence with a history of life in the reserve camps; and, thirdly, those admitted after service in the Philippine Islands. The soldiers admitted to the hospital from service in Cuba and Porto Rico had, with very few exceptions, been discharged before our examinations commenced.

In connection with the above groups of patients, having a history of military service, it will be interesting to compare the 397 male civilians admitted to the Government hospital from the District of Columbia.

The total infections among white males admitted to the Government hospital from military service, from soldiers' homes, and from civil life in the District of Columbia were as follows:^a

	Examined.	Infections.	Per 100 persons.
Soldiers' Homes.....	395	15	3.80
District of Columbia.....	397	22	5.54
Army before 1898.....	179	13	7.26
Navy.....	103	9	8.74
Army after 1898.....	90	19	21.11
Philippine service.....	115	52	45.22

The relative frequency of helminthiasis in the different groups, as set forth in the above figures, is confirmatory of what would be naturally expected from the various histories of the patients in question. In these histories locality and manner of life are probably the most important elements from a parasitological viewpoint, though age and length of institutional life also are contributing factors. Before attempting to discuss the possible relative importance of these separate influences present in the histories of the patients it is desirable to consider the relative frequency of infection with each species of parasite in the above groups:

	Examined.	Infections.	Per 100 persons.
<i>Trichuris trichiura:</i>			
Soldiers' Homes.....	395	6	1.52
District of Columbia.....	397	15	3.78
Army before 1898.....	179	8	4.47
Navy.....	103	7	6.80
Army after 1898.....	90	14	15.55
Philippine service.....	115	36	31.30
<i>Oxyuris vermicularis:</i>			
Soldiers' Homes.....	395	5	1.27
District of Columbia.....	397	3	0.76
Army before 1898.....	179	4	2.23
Navy.....	103	1	0.97
Army after 1898.....	90	1	1.11
Philippine service.....	115	0	0.00
Hookworms:			
Soldiers' Homes.....	395	2	0.51
District of Columbia.....	397	2	0.50
Army before 1898.....	179	0	0.00
Navy.....	103	1	0.97
Army after 1898.....	90	3	3.33
Philippine service.....	115	14	12.17
<i>Ascaris lumbricoides:</i>			
Soldiers' Homes.....	395	1	0.25
District of Columbia.....	397	0	0.00

^a There were 215 white males at the Government hospital who could not be classified in the above groups.

	Examined.	Infections.	Per 100 persons.
<i>Ascaris lumbricoides</i> —Continued.			
Army before 1898.....	179	0	0.00
Navy.....	103	0	0.00
Army after 1898.....	90	1	1.11
Philippine service.....	115	1	0.87
<i>Strongyloides stercoralis</i> :			
Soldiers' Homes	395	1	0.25
District of Columbia.....	397	2	0.50
Army before 1898.....	179	0	0.00
Navy.....	103	1	0.97
Army after 1898.....	90	0	0.00
Philippine service.....	115	1	0.87

Hymenolepis nana and *Tænia saginata* gave no infections in any of the above groups.

The soldiers admitted to the hospital from the Soldiers' Homes in various parts of the country gave the lowest rate of total infection. These patients were, for the most part, men of advanced years. It would seem, therefore, that age and long institutional life were the factors most concerned in causing the low percentage of infection found in this group. This probability is strengthened with regard to the factor of institutional life by the figures for whipworms and pinworms. As has been already mentioned (p. 37), the conditions present in institutional life, while unfavorable to the propagation of infection with an intestinal worm of a more or less complex life cycle, such as that of *Trichuris*, would be especially favorable to the spread of a directly transmissible parasite like *Oxyuris*. Accordingly, whipworms gave a lower rate of infection among the men admitted to the hospital from an earlier period of institutional life in the Soldiers' Homes than in any other of the groups under consideration, while pinworms presented a higher frequency of infection among these patients than in any other group but one.

The civilian patients admitted to the hospital from the District of Columbia presented a higher percentage of total infection than the patients admitted from the Soldiers' Homes, but a lower rate than any group of patients admitted from military service. These facts would seem to indicate that the conditions of life in the general population even of a large city are more favorable to helminthiasis in general than the conditions of such institutional life, and, furthermore, that army life, even in the Regular Army posts, is more conducive to intestinal worms than that of cities. When we consider the infections with whipworms and with pinworms separately, however, the above indications are seen to hold only in the case of the former parasite, since pinworms gave a higher rate of infection among both the old soldiers from the Soldiers' Homes and the soldiers from the Regular Army posts

(Army before 1898) than among the civilians from the District of Columbia. It is possible that the relatively high frequency of pinworms among the soldiers admitted from the Army before 1898 may have the same explanation as that suggested in the case of the soldiers from the Soldiers' Homes, namely, a long period of institutional life. All of the soldiers admitted before the Spanish-American war had necessarily been residents at the hospital at least four years before our examinations were begun.

It is of interest to note that the rate of total infection among patients admitted to the hospital from the Navy is considerably higher than that among patients from civil life in the District of Columbia and slightly higher than the rate among the soldiers admitted from the Army before 1898.

The soldiers admitted to the hospital after the outbreak of the Spanish-American war (1898) gave a rate of total infection almost three times as great as the rate present among soldiers admitted from the Army before that time. It is natural to attribute this marked difference in the frequency of helminthiasis in the two groups to the better hygienic conditions prevailing at the Regular Army posts than at the temporary reserve camps established during the war. Other factors to be considered, however, are the younger average age of the soldiers admitted during and after the war and the greater length of hospital residence prior to the time of examination in the case of the soldiers admitted to the hospital before 1898. It is seen that the higher rate of infection among the men from the Army after 1898 is due almost entirely to a greater frequency of infection with whipworms and with hookworms, while pinworms gave a considerably higher infection among the soldiers admitted before the war.

The soldiers admitted to the Government hospital after military service in the Philippine Islands presented a higher rate of total infection than did any other group of patients examined, excepting the female patients confined to a few wards in one section of the Connecticut hospital (see p. 58). The Philippine soldiers gave more than twice as many infections per 100 persons than did the soldiers admitted to the Government hospital from service in the States during the war and over eight times as many infections as the civilians admitted from the District of Columbia. The parasites contributing to this excessive amount of infection among the Philippine soldiers were for the most part whipworms and hookworms, eelworms and Cochin China worms having presented but one infection each and pinworms none. The most striking results in this group of patients are the relatively high figures for hookworms. Of the 36 infections with this parasite found in the total 3,457 persons examined, 14 occurred in this group of 115 men. It is remarkable that *Ascaris lumbricoides* should have given only one infection among the Philippine soldiers.

According to common report, eelworms were extremely prevalent among the American soldiers in the Philippines, and Strong has reported this parasite as the most common intestinal worm in those islands (see p. 66). The almost total absence of *Ascaris* infections among the Philippine men at the Government hospital would seem to indicate, in view of these reports, that eelworm infections are of comparatively short longevity and that the infections had been lost before the men reached the hospital.

DISTRIBUTION OF INFECTIONS IN WARDS AND BUILDINGS.

Both at the national and the Connecticut hospitals there was extreme variation in the amount of infection in the different buildings and upon the different wards. (Table 2.)

At St. Elizabeth the frequency ranged from 0 to 46.48 infections per 100 patients on the different wards; at Connecticut, from 0 to 75 infections per 100 patients. At the Government hospital, however, where the patients are admitted from such widely separated localities and such diverse conditions of life, it is practically impossible to eliminate these complicating elements associated with their history prior to admission. For example, in the two wards at the national hospital which gave the highest rates of infection (46.48 and 44.12 per 100, respectively), 69 of the 105 men examined were soldiers admitted from active service, and 42 of these had recently returned from the Philippines. Another ward, situated in the same wing of the same building, but on the ground floor, showed no infections among the 42 men examined. Of these latter 42 men, 36 were admitted from the Soldiers' Homes. In each of these cases it seems evident that the history of the men prior to admission had more influence in determining the amount of parasitism than did their ward life. Because of the difficulty in eliminating these complicating elements at St. Elizabeth we have confined our study of the distribution of intestinal parasites by wards to the Connecticut institution, where the patients represent a more uniform history, having been admitted from civilian life and from the comparatively similar climatic and social conditions found within the bounds of the one State.

The 1,010 patients examined at the Connecticut hospital were distributed among 42 wards in 5 buildings. The distribution of the infections with intestinal worms among the 5 buildings was as follows in ascending order of frequency:

	Examined.	Infections.	Per 100 persons.
Building A.....	400	20	5.00
Building B.....	363	42	11.57
Building C.....	171	2	16.96
Building D.....	75	46	61.33

In A, B, and C, males and females occupy opposite ends of the buildings, the men and women being so entirely separated that from our point of view they may be considered as in separate buildings. Building D is devoted entirely to females. We have, then, 7 divisions, showing the following relative amounts of infection, arranged in ascending order:

	Examined.	Infections.	Per 100 persons.
1. [A males].....	195	5	2.56
2. [A females].....	205	15	7.32
3. [B females].....	159	14	8.81
4. [C males].....	102	11	10.78
5. [B males].....	204	28	13.73
6. [C females].....	69	18	26.09
7. [D females].....	75	46	61.33

The only change in the order of buildings in considering the male and female departments separately is in the position of the male section of Building B. The males in this building not only showed a higher rate of infection than the females in the same building, but a higher rate than C males. With this exception, the rate of infection increased in both males and females from A to B, B to C, and C to D, the females in A and C, but not in B, showing a higher rate than the corresponding males.

The amount of infection in the different sections accordingly is found to vary from 2.56 per 100 in the male section of building A to 61.33 per 100 in building D (females).

TABLE II.—*Distribution of infections on wards*

Section.	Sex.	Ward.	Number examined.	Infections.													
				Total.		<i>Trichuris trichiura.</i>		<i>Oxyuris vermicularis.</i>		Hook-worms.		<i>Ascaris lumbricoides.</i>		<i>Strongyloides stercoralis.</i>		<i>Tænia saginata.</i>	
				No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
1	Male.....	1	27	0	0												
		2	18	0	0												
		3	29	0	0												
		4	15	0	0												
		5	12	0	0												
		6	35	1	2.86	0	0	0	0	0	0	1	2.86	0	0	0	0
		7	45	2	4.44	1	2.22	0	0	0	0	1	2.22	0	0	0	0
		8	14	2	14.29	1	7.14	0	0	0	0	0	0	0	0	0	0
		195	5	2.56	2	1.03	1	.51	0	0	2	1.03	0	0	0	0
2	Female.....	1	8	0	0												
		2	10	0	0												
		3	19	0	0												
		4	30	0	0												
		5	28	1	3.57	1	3.57	0	0	0	0	0	0	0	0	0	0
		6	45	3	6.66	2	4.44					1	2.22				
		7	15	2	13.33	2	13.33										
		8	17	3	17.65	3	17.65										
		9	11	2	18.18	2	18.18										
		10	22	4	18.18	3	13.64					1	4.55				
		205	15	7.32	13	6.34					2	.98				
3	Female.....	1	13	0	0												
		2	13	0	0												
		3	25	0	0												
		4	12	1	8.33	1	8.33										
		5	36	3	8.33	3	8.33										
		6	28	3	10.71	1	3.57	1	3.57	1	3.57						
		7	6	1	16.66	1	16.66										
		8	26	6	23.08	5	19.23	1	3.85								
		159	14	8.81	11	6.92	2	1.26	1	.63						
4	Male.....	1	11	0	0												
		2	33	2	6.06	2	6.06										
		3	58	9	15.52	5	8.62	3	5.17					1	1.72		
		102	11	10.78	7	6.86	3	2.94					1	.98		
5	Male.....	1	20	1	5.00			1	5.00								
		2	38	2	5.26			2	5.26								
		3	36	2	5.55	1	2.77										
		4	44	3	6.82	1	2.27	2	4.55								
		5	21	3	14.28	1	4.76	1	4.76					1	4.76		
		6	45	17	37.77	6	13.33	11	24.44								
		204	28	13.73	9	4.41	18	8.82					1	.49		

and in sections at the Connecticut Hospital.

History.												
Age.				Length of residence.						Nativity.		
15-30	31-50	51+	?	-1	1-3	4-8	9-15	15+	?	U. S.	Foreign.	?
7	14	6	0	3	5	6	4	9	0	20	7	0
0	2	15	1	3	10	4	1	0	0	13	5	0
4	18	6	1	8	12	4	0	5	0	23	6	0
3	6	5	1	11	2	0	0	1	1	9	5	1
0	5	7	0	1	4	2	4	1	0	10	2	0
17	15	2	1	8	21	2	2	1	1	28	6	1
10	18	17	0	15	14	10	5	1	0	31	14	0
4	5	4	1	4	6	1	2	0	1	9	5	0
45	83	62	5	53	74	29	18	18	3	145	50	2
0	4	4	0	1	3	3	1	0	0	6	2	0
1	3	6	0	2	2	1	1	4	0	6	3	1
3	5	10	1	3	8	3	3	2	0	16	2	1
3	16	11	0	1	11	11	4	3	0	16	14	0
3	16	9	0	2	8	9	5	4	0	16	11	1
5	24	16	0	8	17	12	6	2	0	30	14	1
0	10	4	1	5	5	3	1	1	0	6	8	1
5	11	1	0	6	7	2	1	1	0	10	7	0
2	7	2	0	6	4	0	1	0	0	5	6	0
4	12	6	0	7	6	5	4	0	0	15	5	2
26	108	69	2	41	71	49	27	17	0	126	72	7
1	5	7	0	0	3	7	3	0	0	10	3	0
0	9	4	0	0	2	1	5	5	0	9	4	0
2	11	12	0	1	7	11	4	2	0	8	17	0
1	2	9	0	0	3	6	2	1	0	8	4	0
0	16	20	0	4	7	17	4	4	0	19	17	0
5	10	13	0	1	10	10	4	3	0	16	11	1
0	3	3	0	0	3	1	1	1	0	2	4	0
4	12	10	0	0	6	12	2	6	0	13	12	1
13	68	78	0	6	41	65	25	22	0	85	72	2
2	5	3	1	2	4	2	1	2	0	8	3	0
5	20	8	0	1	10	9	4	9	0	21	12	0
11	29	17	1	1	17	7	13	19	1	44	13	1
18	54	28	2	4	31	18	18	30	1	73	28	1
4	13	2	1	0	5	9	5	0	1	19	0	1
3	23	10	2	0	10	18	7	1	2	24	12	2
4	16	16	0	4	14	12	3	1	2	26	10	0
7	26	11	0	2	10	22	8	2	0	32	12	0
4	11	5	1	0	6	9	3	2	1	16	4	1
13	23	8	1	2	10	14	17	2	0	28	15	2
35	112	52	5	8	55	84	43	8	6	145	53	6

in sections at the Connecticut Hospital—Continued.

History.												
Age.				Length of residence.						Nativity.		
15-30	31-36	51+	?	-1	1-3	4-3	9-15	15+	?	U. S.	Foreign.	?
0	11	9	0	0	1	4	8	6	1	13	7	0
1	10	6	0	0	0	7	6	4	0	12	5	0
0	9	8	0	0	2	7	0	8	0	6	11	0
0	8	7	0	0	3	1	3	8	0	8	7	0
1	38	30	0	0	6	19	17	26	1	39	30	0
3	12	14	1	2	5	7	4	11	1	11	18	1
0	6	14	1	0	2	2	8	9	0	12	9	0
1	16	7	0	0	3	3	5	13	0	11	13	0
4	34	35	2	2	10	12	17	33	1	34	40	1

By referring to Table 2 it is seen that not only is there this great difference in the frequency of infections between the various buildings and sections, but that the wards as well in any one section show a wide range in the amount of infection which they present. It must be borne in mind, however, that in considering the patients by wards we are working upon small bases and that the presence or absence of but one or two infections may make a large difference in the rate per cent. In section 1, for instance, 5 of the 8 wards show no infections, and the three infected wards present 2.86, 4.44, and 14.29 infections per 100, respectively, yet the comparatively high rate of 14.29 per 100 represents but 2 infections.

Nevertheless, it can not be considered without significance that, as occurs in section 5, one ward of 44 patients should give only 3 infections (6.82 per 100) and another ward of 45 patients 17 infections (37.77 per 100) or, as in section 3, that a ward of 25 patients should have no infections while a contiguous ward of 26 patients has 6 infections (23.08 per 100).

In sections 6 and 7, all the wards show a high rate of infection, but here also there is a difference of over 35 per 100 in the former section and over 20 infections per 100 in the latter, between the wards giving the lowest and highest rates of infection.

It is evident, therefore, that there is an actual and not insignificant difference in the degree of prevalence of intestinal worms both in the various buildings, sections of a building, and wards of a section, a difference which seems too large and too striking to be wholly explained by any chance distribution of intestinal worms in the institution.

We have made every endeavor to discover an explanation of these conditions, which might have an important influence upon the results of our work. In these endeavors we have been in only a small measure successful.

The great number of infections found among the specimens collected from certain wards led to the suspicion that the stools were contaminated or confused during their collection. Such contamination was rendered very improbable by the fact that the number of eggs present in the specimens collected on the same day from different patients varied greatly; further, the possibility of contamination was later excluded by personally collecting and reexamining specimens from these wards.

The only parasites which present infections in sufficient numbers to be considered separately in this connection are the whipworm and pinworm.

Of the 26 infections with *Oxyuris* found among the 1,010 Connecticut cases, 18 appeared in one section (section 5) of 204 men, the other 8 infections being distributed among 4 other sections. Furthermore 11 of the 18 infections in section 5 occurred among the 45 men on ward

6, and the 7 remaining infections were distributed in the other 5 wards of this section.

Ward 6 of section 5, therefore, with 11 infections (24.44 per cent) with *Oxyuris* among its 45 patients, while the remaining 41 wards of the hospital with 965 patients gave only 15 infections (1.55 per cent) rather evenly distributed among them, presents a striking illustration of the unequal distribution of infections above noted. It will be seen that of the total 26 infections, 18 were in section 5, and 22 were in males.

In the case of *Oxyuris* infection on section 5, the condition of affairs presented seems to be in harmony with our knowledge of the life cycle of the parasite and of its direct transmissibility; further, this section is distinctly separated from the other sections of the hospital and the patients of the various wards of section 5 come into closer contact with each other than they do with patients from any other section. It may further be noted that in section 4 all 3 cases of pinworm infection found among the 102 patients were confined to ward 3, having 58 patients; this condition gives rise to the suspicion that *Oxyuris* may be spreading in this ward.

The infections with *Trichuris* are more generally distributed among the wards, but scarcely more equally. No section is free from this parasite. The rate of infection on the different sections varied, however, from 1.03 to 53.33 per cent, and while 16 wards showed no whipworm infections, one ward showed 75 per cent and 3 other wards showed 40, 47.61, and 53.33 per cent, respectively. The most remarkable congregation of *Trichuris* infections appeared in sections 6 and 7. While on no other section did the rate of infection go above 6.92 per cent, section 6 presented 26.09 per cent and section 7 presented 53.33 per cent; and while the highest rate found on any one ward in any of the other sections was 19.23 (ward 8, section 3), the 4 wards of section 6 gave 15, 17.65, 23.53, and 53.33 per cent, and the 3 wards of section 7 showed 40, 47.61, and 75 per cent of infection.

This unequal distribution of *Trichuris* infections seems to find no explanation in the mode of transmission of the parasite. On the contrary, the period of incubation proved experimentally to be demanded by the *Trichuris* egg, before hatching, excludes the possibility of this infection being transmitted directly from patient to patient upon a ward or in a section of a building, in the same sense as may take place in the case of *Oxyuris*.

Buildings heavily or lightly infected received the same water supply and, in conjunction with the hospital staff, we were not able to discover any conditions in the sanitary arrangements in the different sections and wards which would in any way account for the very much greater prevalence of *Trichuris* in some than in others.

With the thought that the factors of sex, age, institutional life, and nativity might separately or in combination offer some explanation

of the higher rate of infection on certain wards, we have brought together in Table 2, the amount of infection upon each ward and in each section, together with the history of the patients with regard to the above points.

In our total results it was noted that women were more frequently infected (10.21 per 100) than men (6.45 per 100) and that this sex inequality was especially marked among the Connecticut cases taken separately, the Connecticut women giving 17.72 infections per 100 and the Connecticut men 8.96 infections per 100.

As would be expected, accordingly, we find the most heavily infested wards are female wards. The highest rate of infection found on any male ward was 37.77 per 100 and the next 3 highest male wards showed only 15.52, 14.29, and 14.28 per 100, respectively, while among the women the 4 highest wards gave, respectively, 75, 57.14, 53.33, and 53.33 per 100. Two other female wards showed 23.08 and 23.56 per 100, and still 6 others showed 15 per 100 or over.

It is evident, then, that differences in ward infection may be due in part at least to that greater tendency to intestinal worms among women which we have already noted in our general results.

That this is not the entire explanation, however, is at once apparent when we consider that among the female wards alone the variation in the amount of infection was no less striking. Seven female wards showed no infections, and on the remaining 18 female wards the amount of infection varied from 3.57 to 75 per 100 patients. Furthermore, while we have besides the 7 uninfected female wards, 4 female wards which gave less than 10 infections per 100 (5.57, 6.66, 8.33, and 8.33 per 100), there are 3 male wards which gave about 15 infections per 100 (15, 14.29, 14.28 per 100) and one male ward giving 37.77 infections per 100. It is evident also from the figures already given that there is a variation of from 2.86 to 37.77 infections per 100 on the infected male wards alone, and 6 male wards are uninfected.

Evidently there is a wide range in the amount of infection upon the various wards wholly independent of what might be explained by the greater frequency of intestinal parasites among women.

Taking up the consideration of the age and nativity of the patients and the length of time they had been in the hospital, it must be borne in mind that the variation in the amount of infection due to each of these factors, as appears in our previous pages, is too small to account for the wide difference which we found in the amount of infection upon the separate wards and sections, and that if the relatively high percentage of infections found upon certain wards was due in any considerable degree to any conditions of age, nativity, or length of institutional life among the patients upon those wards, these conditions must be present in combination and in a very apparent and striking manner.

Though we have studied Table 2 carefully, a mere glance is sufficient

to show approximately to what extent a combination of conditions exists. Following the age column from section 1 (lightly infected) to section 7 (heavily infected), it is apparent that the proportion of younger patients decreases as we pass to the more heavily infected sections; indeed, it is considerably less in the sections (6 and 7) showing the highest rates of infection than in those (1 and 2) showing the lowest. Since we have found the relation between age and the rate of infection to differ in the two sexes at the Connecticut hospital (see pp. 26, 27), it is significant that this tendency to a greater proportion of older patients on the heavily-infested sections is confined for the most part to the female sections, the male sections showing but little variation in the proportionate number of patients of different ages.

Considering the length of time that the patients had been in the hospital, we find that the proportion of patients of long hospital residence increases with the rate of infection. In section 1, with only 2.56 per cent of infections, over 65 per cent of the patients had been admitted to the hospital within three years. Sections 6 and 7, with 26.09 and 53.33 per cent of infections, show in the one case about 60 per cent and in the other 66 per cent of the patients with a hospital residence of over nine years.

Regarding the nativity of the patients, there is a higher proportion of foreign-born patients upon the 2 sections having a higher rate of infection than upon the more lightly infected sections, and the conditions in other sections also seem to be in general in harmony with the data of the sections in question.

In section 1 it is seen that 143 of the 195 patients are native Americans. In section 7, 40 of the 75 patients are of foreign birth. While there is this general tendency to a higher proportion of foreign-born patients upon the sections showing the higher rates of infection, there is a marked exception in section 5, the most highly infected male section (13.73 per 100), which, with 145 native and 53 foreign born, presents about the same proportion as does section 1. It is worthy of note, however, that this single exception to the general tendency above noted is the one section upon which the pinworm furnished most of the infections, and the pinworm we have already found to show a slightly higher prevalence among natives (see p.44).

In general, then, we find upon the sections showing the higher frequency of intestinal worms a tendency to a greater proportion of patients of long institutional life, of foreign birth, and, particularly among the females of advanced age as well, conditions which we have already found to be apparently predisposing to intestinal worms, especially among the Connecticut cases.

The question naturally follows whether the combined influence of sex, age, nativity, and length of hospital life is sufficient to explain the wide differences in the amount of infection found in the various wards and sections.

This question can be answered only approximately. At the Connecticut hospital we found a difference of about 9 per cent between the amount of infection present among males and among females; about 10 per cent may be due to a difference in age, about 5 per cent to a difference in the length of institutional life, and about 2 per cent to nativity. The proper combination of these conditions, therefore, might be held accountable, perhaps, for a maximum difference of from 20 to 30 per cent in the frequency of infection upon the different wards and sections. The range of the rate of infection upon the different wards is from 0 to 75 per cent and upon the different sections from 2.56 to 61.33 per cent. There remains, therefore, from 30 to 45 per cent of variation in the amount of infection upon the different wards and sections which could not be explained by any combination of sex, age, nativity, or length of hospital life.

As we find these factors in only a very imperfect combination upon our wards, it is probable that they can be held accountable in only a small measure for the unequal distribution of infection among the wards. Since no conditions, sanitary or administrative, were found which would account for more infection upon one ward than upon another, and since the unequal distribution of infections has not been adequately explained by conditions of sex, age, length of institutional life, or nativity, we must content ourselves with the mere presentation of the facts as they appear.

RESULTS OF FORMER INVESTIGATIONS.

In Table 3 we have brought together most of the statistics at our command concerning the frequency of intestinal worms in man. It is difficult to draw any comparisons between these different results. The very high percentage of infection found in some investigations is due to an endemic condition with a certain worm in the locality in question, in others to a selection of cases. It is notable, however, that our own results show the lowest total rate (11.17 per 100) of infection, the 14.07 per 100 reported by Mueller from 1,939 autopsies made at Dresden being the next lowest. From these figures the rate of infection varies through almost all degrees until it reaches its maximum (139.65 per 100) among the 4,482 anemics examined by Ashford, King, and Gutierrez in Porto Rico.

There is also a marked variation in the relative frequency of the different worms as given by the different authors. A glance at the table shows that the three nematodes, *Trichuris*, *Ascaris*, and *Oxyuris*, give the great majority of the infections. The hookworm is the most common parasite in the Porto Rican statistics (100 per cent), in those of Dobson (75.78 per cent) and of Fearnside (65.83 per cent) in India, and of Daniels in British Central Africa (9.96 per cent). Boycott (4.08 per cent) and Strong (2.48 per cent) are the only additional authors besides ourselves (1.04 per cent) who give data for this worm.

Kessler found *Dibothriocephalus latus* the most common intestinal worm at St. Petersburg, and this parasite figures more or less prominently in all the Russian statistics, being present in as high as 10. and 16.92 per cent at Dorpat and Kostroma; the only statistics found for this worm in tropical regions are those of Wellman, who reports 4 cases (1.29 per cent) among 310 natives examined antemortem in Angola, West Africa.

The relative frequency of *Trichuris*, *Ascaris*, and *Oxyuris* also varies considerably, though the last is rarer than the other two in all but three cases, Dobson, Kessler, and Banik alone finding a higher percentage of infection with *Oxyuris* than with *Trichuris* or *Ascaris*. The figures presented in the table emphasize the fact that *Trichuris* and *Ascaris* are man's most common and most widely-distributed intestinal worms, and are almost equally prevalent. Eleven authorities give a higher percentage of infection with *Trichuris* and 12 find a higher rate with *Ascaris*.

TABLE III.—Statistics of the frequency of intestinal worms in man, reported by different authors.

Authority; locality; date of publication or of examination.	Number of subjects examined.	Infected.		Infections.			
				<i>Trichuris trichiura</i> .		<i>Oxyuris vermicularis</i> .	
		Number.	Percent.	Number.	Percent.	Number.	Percent.
Stiles & Garrison, United States, 1906.	3,457	349	10.10	267	7.72	45	1.30
Ashford, King & Gutierrez, Porto Rico, 1904	4,482	4,482	100.00	326	7.27	3	0.07
Boycott, Cornwall, England, 1904	98			38	38.78	2	2.04
Wellman, West Africa, 1904	310						
Daniels, British Central Africa, 1901.	251			7	2.79		
Strong, Philippine Islands, 1901	2,179			Very common.		Several cases.	
Calvert, India, 1901	100	92	92.00	12	12.00	9	9.00
Fearnside, India, 1900	878			61	6.95		
Cima, Italy, 1893 and 1896	110	50	45.45	41	37.27	7	6.36
Gubareff, Russia, 1896	486	325	66.87	212	43.62	4	0.82
Heisig, Greifswald, 1893	230	114	49.56	104	45.21	No ova. Worms common.	
Dobson, India, 1893	1,249			55	4.40	192	15.37
Grusdeff, Kostroma, Russia, 1892	260	119	45.77	6	2.31	6	2.31
Grechaninoff, St. Petersburg, 1890	583	337	57.80	154	26.41	64	10.98
Baranovski, Moscow, 1889	1,000	331	33.10	53	5.30	80	8.00
Kessler, St. Petersburg, 1888	600			30	5.00	43	7.16
Sievers, Kiel, Germany, 1887	2,629			521	19.81	326	12.40
Friedrich, München 1887	107	19	17.76	10	9.34	3	2.80
Banik, München, 1886	315	126	40.31	26	8.25	95	30.16
Szydlowski, Dorpat, 1879					4.00		0.00
Roth, Bâle, Germany, 1877-1880	752			178	23.67		
Gribbohm, Kiel, Germany, 1872-1877	972	484	49.80	313	32.20	226	23.30
Heller, Kiel, Germany, 1872-1875	611	291	47.62	187	30.60	142	23.25
Cruse, Dorpat, 1872	482						
Müller, Erlangen, Germany, 1862-1873	1,755			195	11.11	213	12.13
Müller, Dresden, Germany 1852-1862	1,939			50	2.57	43	2.21

TABLE III.—Statistics of the frequency of intestinal worms in man, reported by different authors—Continued.

Authority; locality; date of publication or of examination.	Infections.									
	Hook-worms.		<i>Ascaris lumbricoides.</i>		<i>Strongyloides stercoralis.</i>		<i>Hymenolepis nana.</i>		<i>Tænia saginata.</i>	
	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Stiles & Garrison, United States, 1906.	36	1.04	17	0.49	8	0.23	12	0.35	2	0.06
Ashford, King & Gutierrez, Porto Rico, 1904.....	4,482	100.00	1,408	31.41	36	0.80	3	0.07
Boycott, Cornwall, England, 1904.....	4	4.18	12	12.24	0	0.00
Wellman, West Africa, 1904.....	13	4.19	158	50.97	2	0.65	2	0.65
Daniels, British Central Africa, 1901..	25	9.96	15	5.98	3	1.20
Strong, Philippine Islands, 1901.....	54	2.48	Most common intestinal worm.		13	0.60	Present.	
Calvert, India, 1901.....	83	83.00	39	39.00
Fearnside, India, 1900.....	578	65.83	282	32.12
Cima, Italy, 1893 and 1896.....	31	28.18	7	6.36	1	0.91
Gubareff, Russia, 1896.....	110	22.63	78	1.64
Heisig, Greifswald, 1893.....	34	14.78	1	0.43
Dobson, India, 1893.....	944	75.58	131	10.49	18	1.44
Grusdeff, Kostroma, Russia, 1892.....	86	33.08
Grechaninoff, St. Petersburg, 1890.....	218	37.39
Baranovski, Moscow, 1889.....	101	10.10	26	2.60
Kessler, St. Petersburg, 1888.....	35	5.83	22	3.66
Sievers, Kiel, Germany, 1887.....	436	16.58	8	0.30
Friedrich, München, 1887.....	7	6.54
Banik, München, 1886.....	23	7.30	4	1.27
Szydlowski, Dorpat, 1879.....	25.00
Roth, Bâle, Germany, 1877-1880.....	86	11.43
Gribbohm, Kiel, Germany, 1872-1877..	178	18.31
Heller, Kiel, Germany, 1872-1875.....	108	17.67
Cruse, Dorpat, 1872.....	50	10.37
Müller, Erlangen, Germany, 1862-1873.	227	12.93
Müller, Dresden, Germany, 1852-1862.	180	9.28

TABLE III.—Statistics of the frequency of intestinal worms in man, reported by different authors—Continued.

Authority; locality; date of publica- tion or of examination.	Infections.						Post or ante mortem.
	<i>Tænia solium.</i>		<i>Dibothrio- cephalus latus.</i>		Total infec- tions.		
	Num- ber.	Per cent.	Num- ber.	Per cent.	Num- ber.	Per cent.	
Stiles & Garrison, United States, 1906.	0	0.00	0	0.00	387	11.19	Ante.
Ashford, King & Gutierrez, Porto Rico, 1904	1	0.02	6,259	139.64	Ante.
Boycott, Cornwall, England, 1904....	0	0.00	56	57.24	Ante.
Wellman, West Africa, 1904.....	4	1.29	179	57.75	Ante.
Daniels, British Central Africa, 1901..	50	19.93	Ante.
Strong, Philippine Islands, 1901.....	Present.		Ante and post.
Calvert, India, 1901.....	143	143.00	Ante.
Fearnside, India, 1900.....	921	104.90	Ante.
Cima, Italy, 1893 and 1896.....	0	0.00	87	79.08	Ante and post.
Gubareff, Russia, 1896.....	24	0.82	33	6.79	371	76.32	(?)
Heisig, Greifswald, 1893.....	1	0.43	140	60.85	Ante.
Dobson, India, 1893.....	1,340	107.28	Ante.
Grusdeff, Kostroma, Russia, 1892....	1	0.38	44	16.92	143	55.00	Ante.
Grechaninoff, St. Petersburg, 1890....	4	0.68	440	75.47	Ante.?
Baranovski, Moscow, 1889.....	11	1.10	89	8.90	360	36.00	Ante.?
Kessler, St. Petersburg, 1888.....	18	3.00	47	7.83	195	32.48	Ante.
Sievers, Kiel, Germany, 1887.....	1,291	49.09	Post.
Friedrich, München, 1887.....	20	18.68	Post.
Banik, München, 1886.....	1	0.32	149	47.30	Post.?
Szydlowski, Dorpat, 1879.....	Rare.		10.00	39.+	Ante.
Roth, Bâle, Germany, 1887-1880.....	264	35.10	Post.
Gribbohm, Kiel, Germany, 1872-1877..	717	73.81	Post.
Heller, Kiel, Germany, 1872-1875.....	437	71.52	Post.
Cruse, Dorpat, 1872.....	1	0.20	29	6.00	80	16.57	Post.
Müller, Erlangen, Germany, 1862-1873..	635	36.18	Post.
Müller, Dresden, Germany, 1852-1862..	273	14.07	Post.

The Philippine Islands (0.6 per cent), Porto Rico (0.8 per cent), British Central Africa (1.30 per cent), and our own (0.23 per cent) are the only localities from which statistics could be obtained for *Strongyloides stercoralis*, and, except the 0.35 per cent of infections found among our own cases, Cima's report of 6.36 per cent among 110 children examined in Italy are the only exact figures available for the dwarf tapeworm, *Hymenolepis nana*.

The two species of *Tænia* (*T. saginata* and *T. solium*), while never present in a high proportion of cases, are widely distributed and fairly constant, the percentage varying from 0.06 to 3.66 for the beef tapeworm and from 0.02 to 3 for *T. solium*. The latter ^a is seen to be almost invariably the rarer of the two worms.

It would appear as if the prevalence of hookworms, of *Strongyloides stercoralis*, of *Dibothriocephalus latus*, and of *Hymenolepis nana* is governed largely by local conditions, and that these parasites tend to a high degree of frequency in more limited areas, while *Trichuris*, *Oxyuris*, *Ascaris*, and the two *Tæniæ* seem to be practically of world-wide and comparatively even distribution.

We have found other statistical references to the frequency of helminthiasis in different localities which are not included in Table 2. Among them are the following:

Rœderer,^b Gottingen, *Trichuris*, 13 persons examined, 6 (46.15 per cent) infected; Cooper,^b Greenwich, *Trichuris*, 16 persons examined, 11 (68.75 per cent) infected; Bellingham,^c Dublin, *Trichuris*, 29 examined, 26 (89.65 per cent) infected; Erni,^d Malayan Archipelago, *Trichuris*, 30 persons examined, 24 (80 per cent) infected; Vix, Hopheim Asylum, 86 insane patients examined, 40 (46 per cent) infected with *Trichuris*,^b 56 (60 per cent) infected with *Oxyuris*,^e 18 (21 per cent) infected with *Ascaris*,^f *Ascaris* present also in 8 per cent of sane persons examined; Vital,^g Constantine, *Ascaris*, 1 in 7 of the natives and 1 in 33 of the Europeans infected; Sandwith,^h hookworms, 3.3 per cent of the population infected in Upper Egypt, 6.2 per cent in Lower Egypt, 13.9 per cent in Menonfieh; Zinn and Jacoby,ⁱ West Africa, 23 negroes examined, 21 infected with *Agchylostoma duodenale*, 8 with *Trichuris*, 8 with *Ascaris*, 4 with *Strongyloides*, and 4 with *Tænia*; Zaeslein, Bâle, 752 autopsies, 178 (23.7 per cent) infected with *Trichuris*,^b 86 (11.4 per cent) infected with *Ascaris*,^c and *Oxyuris* ^j present in 10 of 50 consecutive autopsies (20 per cent); in Paris^d and in Southern Italy,^k *Trichuris* has been estimated to be present in from 50 to nearly 100 per cent of the population; Sommer^l found *Trichuris*

^a In this part of the United States *T. saginata* is the usual large tapeworm found.

^b Blanchard, 1888a, 783.

^c Bellingham, 1838a, 346-347.

^d Blanchard, 1888a, 785.

^e Blanchard, 1888a, 722.

^f Blanchard, 1888a, 689.

^g Blanchard, 1888a, 688.

^h Looss, 1894, 3 footnote.

ⁱ Zinn and Jacoby, 1896, 2.

^j Blanchard, 1888a, 724.

^k Braun, 1903, 279.

^l Sommer, 1895, 353-354.

in 11.11 per cent of 36 children examined in the District of Columbia in 1895.

The various reports of special outbreaks of uncinariasis among miners, brick makers, etc., do not as a rule furnish good statistical material. In the Westphalian coal mines of Germany official statistics show (Boycott and Haldane, 1904, 105-106) that of 188,730 miners employed in the district 17,101 (9.10 per cent) were infected with *Agchylostoma duodenale* at the beginning of the campaign against the disease; 63,000 men who worked in collieries which were declared infected with the parasite showed 12,157 infections, or 19.3 per cent; under the energetic measures initiated the rate of infection in the infected collieries rapidly fell to 7.60 per cent. These figures are not included in the statistical summaries given below.

There are a number of other places in which the population is known to be more or less generally infested with certain parasitic worms of the intestine, but for which we have no definite statistics.

The most striking difference which appears, if we make a general comparison between our own results and those quoted, is the lower rate of infection among our cases. In the total number of infections, and almost always in the number of infections with each parasite as well, our percentages are lower than those given by any other investigators.

On the other hand, our results differ from all but a few other researches in giving figures for *Hymenolepis nana*, *Strongyloides stercoralis*, and for the hookworm.

The whipworm (*Trichuris trichiura*) forms a larger proportion of the infections in our findings than in those of other authors.

With regard to the relation between sex and the prevalence of intestinal worms found in the results of other investigations, we have summarized below the available statistics for each species of parasite in males and in females. This summary includes all cases examined by each author quoted in Table 3, so far as figures were given for the two sexes separately, except the Porto Ricans examined by Ashford, King, and Gutierrez; these Porto Rican statistics gave the proportion of infected males and females which appeared at the clinics of the commission, but not necessarily the relative frequency of infection in males and in females in the general population (see p. 30).

	Examined.	Infected.	Per 100 persons.
<i>Trichuris trichiura</i> :			
Males.....	1,543	267	17.30
Females.....	810	165	20.37
<i>Ascaris lumbricoides</i> :			
Males.....	1,732	138	7.97
Females.....	1,103	159	14.42
<i>Oxyuris vermicularis</i> :			
Males.....	1,543	178	11.54
Females.....	810	115	14.20
<i>Tænia saginata</i> :			
Males.....	846	20	2.36
Females.....	324	19	5.86
<i>Tænia solium</i> :			
Males.....	846	15	1.77
Females.....	324	7	2.16
<i>Dibothriocephalus latus</i> :			
Males.....	846	51	6.03
Females.....	324	59	18.21
All intestinal worms:			
Males.....	2,008	672	33.47
Females.....	1,191	531	44.58

It appears from the above figures that the females gave a higher percentage of infection than the males, both in the rate of total infection and in the rate of infection with each species of intestinal worm for which statistics for the two sexes were available. In the total results for all parasites considered, males gave about three-fourths as many infections per 100 persons as did the females. The excess of infection among female patients varied in the different species. *Dibothriocephalus* gave something over three times as many infections per 100 persons among the females as among the males, and *Ascaris* nearly twice as many; in the cases of the other species considered the difference between the rates of infection in the two sexes was less pronounced.

It has been a more difficult matter to summarize the results of other investigations regarding the relation found to exist between age and the prevalence of worms in the intestine, because of the fact that the age-groups of different authors do not correspond—that is, they do not include the same years. For instance, Grusdeff's group of patients from 9 to 18 years of age can not be combined with either of Baranovski's groups of from 10 to 15 or from 15 to 20 years. If we place these three groups together in the larger group of from 9 to 20 years the same difficulty arises, since this group overlaps several other groups, 5 to 10 years, 15 to 30 years, etc., arranged by other authors.

By the following arrangement, however, we have managed to include most of the statistics of the prevalence of *Trichuris*, *Oxyuris*, and *Ascaris* at different ages as reported by various authors.^a

	Examined.	Infected.	Per cent.
<i>Trichuris trichiura:</i>			
0-1 year.....	66	0	0.00
1-3 years.....	64	1	1.56
0-5 years.....	228	16	7.02
3-5 years.....	61	6	9.84
5-10 years.....	203	52	25.62
0-15 years.....	2,381	400	16.80
5-15 years.....	427	101	23.65
10-15 years.....	224	49	21.88
15-20 years.....	121	3	2.48
15-30 years.....	733	41	5.59
20-30 years.....	255	16	6.27
30-40 years.....	232	19	8.19
30-50 years.....	728	66	9.07
40-50 years.....	139	12	8.63
50-60 years.....	78	6	7.69
50-70 years.....	108	9	8.33
50+ years.....	226	16	7.08
60-70 years.....	30	3	10.00
70-80 years.....	10	0	0.00
70+ years.....	13	0	0.00
80+ years.....	3	0	0.00
<i>Ascaris lumbricoides:</i>			
0-1 year.....	66	0	0.00
1-3 years.....	64	3	4.68
0-5 years.....	228	17	7.46
3-5 years.....	61	3	4.92
5-10 years.....	203	47	23.15
0-15 years.....	2,381	444	18.65
5-15 years.....	427	94	22.01
10-15 years.....	224	47	20.98
15-20 years.....	121	21	17.36
15-30 years.....	733	50	6.82
20-30 years.....	255	6	2.35
30-40 years.....	232	15	6.47
30-50 years.....	728	35	4.81
40-50 years.....	139	4	2.88
50-60 years.....	78	1	1.28
50-70 years.....	108	2	1.85
50+ years.....	226	5	2.21
60-70 years.....	30	1	3.33
70-80 years.....	10	0	0.00
70+ years.....	13	1	7.69
80+ years.....	3	1	33.33
<i>Oxyuris vermicularis:</i>			
0-1 year.....	66	0	0.00
1-3 years.....	64	17	26.56
0-5 years.....	169	25	14.79

^a Heavy-faced type indicates the age-groups which correspond in years to those into which our own patients were divided.

	Examined.	Infected.	Per cent.
<i>Oxyuris vermicularis</i> —Continued.			
3-5 years.....	61	21	34.43
5-10 years.....	144	41	28.47
0-15 years.....	1,272	305	23.97
5-15 years.....	324	95	29.32
10-15 years.....	114	19	16.67
15-20 years.....	113	14	12.39
15-30 years.....	368	20	5.43
20-30 years.....	255	6	2.35
30-40 years.....	232	13	5.60
30-50 years.....	371	16	4.31
40-50 years.....	139	3	2.16
50-60 years.....	78	1	1.28
50-70 years.....	108	3	2.78
50+ years.....	121	3	2.48
60-70 years.....	30	2	6.66
70-80 years.....	10	0	0.00
70+ years.....	13	0	0.00
80+ years.....	3	0	0.00

In this arrangement of the age-groups it appears that in the case of each of the three parasites considered a very much higher rate of infection occurs among persons under 15 years of age than in any group above that age. Where the groups are less extensive, and the persons less than 15 years old are divided into those under 5 years and those above 5 years, a very much higher rate of infection is found in the latter group, namely, in children from 5 to 15 years old; *Oxyuris*, however, shows a relatively higher frequency of infection in the younger group, comprised of children under 5 years of age, than does either *Trichuris* or *Ascaris*.

The highest rates of infection with *Trichuris* and with *Ascaris* appear in the two age-groups of from 5 to 10 and from 10 to 15 years, the rate in the former (younger) group being slightly greater than that in the latter. *Oxyuris* presents its highest rate in a still younger group, namely, 3 to 5 years, though there is no group between 1 and 15 years which does not show a much higher frequency with this worm than does any group above 15 years.

We have reports of a number of infections in infants of less than one year, but none is sufficiently statistical in character to be properly included in our tables.

RELATION OF WHIPWORMS TO TYPHOID FEVER.

Within recent months the point has been raised that whipworms may play in typhoid fever a rôle somewhat similar to that ascribed to fleas in connection with plague. With regard to this view it is interesting to compare the percentages of infection with this worm in the

white and the negro in the District of Columbia with the typhoid statistics for the two races.

At the Government hospital the negroes presented a whipworm infection of 9.79 per cent, and 746 whites of similar history showed an infection of 3.75 per cent. If, now, the whipworm infection at St. Elizabeth even approximately represents the relative whipworm infection for the two races in the District of Columbia, and if, further, whipworms play any rôle in typhoid, one might expect to find typhoid to be distributed in the whites and negroes here in approximately the same proportion as are whipworms.

For the year 1903 the District Medical Sanitary Inspector (Walsh, 1904, 54) reports a higher percentage of typhoid among the whites than among the negroes, namely, 3.78 per 1,000 white inhabitants and 3.08 per 1,000 negroes. Thus the district typhoid statistics for 1903 are not in harmony with the whipworm statistics for St. Elizabeth for approximately the same period. On basis of the typhoid reports it must therefore be concluded that either the whipworm statistics of St. Elizabeth Hospital, in reference to race, are directly opposite to the general statistics in the population at large for this locality (a conclusion not in harmony with other examinations which have been made here) or that the theory of the existence of a relation between whipworms and the infection with typhoid receives no support from our statistics of the relative frequency of whipworms among the whites and negroes.

The lethality of typhoid in the District of Columbia is, however, greater among the negroes (19.35 per cent) than among the whites (10.69 per cent). This fact gives rise to the question whether the statistics on the relative frequency of this disease in the white and in the negro are not misleading. Is this higher death rate among negroes due to later diagnosis and inferior nursing, or to the failure to recognize and report the lighter cases—cases which might be more promptly recognized among the whites? On the other hand, is the higher rate of occurrence and the lower lethality of typhoid reported for the whites influenced by the inclusion of any cases of other diseases, such as malaria, in the typhoid statistics? These are questions to which we do not feel justified in giving a definite answer at present.

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WALTER WYMAN, Surgeon-General.

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A STUDY OF THE CAUSE OF SUDDEN DEATH
FOLLOWING THE INJECTION OF
HORSE SERUM.

BY

M. J. ROSENAU

AND

JOHN F. ANDERSON.



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A STUDY OF THE CAUSE OF SUDDEN DEATH FOLLOWING THE INJECTION OF HORSE SERUM.

April 1906

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It has long been known that the blood of certain animals is poisonous when transfused or injected into certain other species.

Many instances might be cited showing that the blood serum of one animal has poisonous properties when injected into an animal of another species. But the blood serum of the horse apparently lacks such poisonous action. Very large quantities of the blood serum of the horse may be injected into man, rabbits, guinea pigs, and many other animals without serious inconvenience, except occasionally a slight reaction at the site of inoculation.

In a certain proportion of cases the injection of horse serum into man is followed by urticarial eruptions, joint pains, fever, swelling of the lymph nodes, edema, and albuminuria. This reaction, which appears after an incubation period of eight to thirteen days, has been termed by Pirquet and Schick the "serum disease."

In exceptional instances sudden death has followed an injection of horse serum in man.

These studies were taken up in October, 1905, in order to throw light upon the cause of this unfortunate accident. We have shown that ordinarily horse serum is a comparatively bland and harmless substance when injected into certain animals; but these animals may be rendered so susceptible that an injection of horse serum may produce sudden death or severe symptoms. For example, large quantities of horse serum may be injected subcutaneously or into the peritoneal cavity of a guinea pig without apparently causing the animal the least inconvenience. However, if a guinea pig is injected with a small quantity, say $\frac{1}{2}$ c. c., of horse serum and after the

expiration of a certain interval is again injected with horse serum the result will probably be fatal. The first injection of horse serum has sensitized the animal in such a way as to render it very susceptible to a toxic principle in horse serum. It is probable that when the guinea pig is injected with the first, or sensitizing, quantity of serum the strange proteid contained in the horse serum develops in the body of the guinea pig "antibodies" which, when brought into contact with more horse serum given at a second injection, produce either a union or a reaction, which causes the toxic action.

A certain time is necessary to elapse between the first and second injections of horse serum before this toxic action is able to manifest itself. This "period of incubation" is from ten to twelve days, and corresponds suggestively with the period of incubation of the serum disease which Pirquet and Schick place at eight to thirteen days.

Guinea pigs may be sensitized with exceedingly small quantities of horse serum. In most of our work we used quantities less than $\frac{1}{250}$ c. c. and we found in one instance that $\frac{1}{1,000,000}$ c. c. of horse serum was sufficient to render a guinea pig susceptible.

It also requires very small quantities of horse serum, when given in a second injection, to produce poisonous symptoms. One-tenth c. c. injected into the peritoneal cavity is sufficient to cause the death of a half-grown guinea pig. One-tenth c. c. of horse serum injected subcutaneously is sufficient to produce serious symptoms. The fact that this toxic action may be developed by such small quantities of serum and the fact that exceedingly small quantities are sufficient to produce symptoms and death upon a second injection, a priori places both the sensitizing and the toxic principle in the horse serum in the "haptin group" of substances in the sense used by Ehrlich.

A still further indication that the side-chain theory in its broadest sense may be applicable is the further fact that immunity may be produced against the toxic action by multiple injections of the serum.

While at first we thought that diphtheria antitoxin had some relation to this action, we are now able to state positively that it has nothing whatever to do with the poisonous action of horse serum; further, that diphtheria antitoxin in itself is absolutely harmless. The toxic action which we have studied is caused by a principle in normal horse serum and is entirely independent of the antitoxic properties of the serum.

Part I.

CONTROL EXPERIMENTS.

ACTION OF NORMAL HORSE SERUM UPON NORMAL GUINEA PIGS.

Normal horse serum when injected into normal guinea pigs causes no symptoms. Large amounts, such as 6 or 10 c. c., may be injected into the peritoneal cavity of a guinea pig without any apparent inconvenience to the animal. When normal horse serum is injected subcutaneously into the guinea pig it is sometimes either absorbed very slowly or there is a slight local reaction, as indicated by edema and induration of the subcutaneous tissue at the site of injection.

G. P. No. 2.^a Six c. c. normal horse serum (roan horse) injected into the peritoneal cavity.
No symptoms.

G. P. No. 3. Ten c. c. normal horse serum (roan horse) injected into the peritoneal cavity.
No symptoms.

G. P. No. 63. Six c. c. normal horse serum (Sp. horse) injected into the peritoneal cavity.
No symptoms.

G. P. No. 64. Six c. c. normal horse serum (Jane horse) injected into the peritoneal cavity.
No symptoms.

G. P. No. 66. Six c. c. normal horse serum (Sam horse) injected into the peritoneal cavity.
No symptoms.

G. P. No. 65. Six c. c. normal donkey serum (donkey No. 58) injected into the peritoneal cavity. No symptoms.

G. P. No. 296. Six c. c. normal donkey serum injected into the peritoneal cavity. No symptoms.

G. P. No. 297. Do.

G. P. No. 298. Six c. c. normal horse serum (Sp.) injected into the peritoneal cavity. No symptoms.

G. P. No. 299. Do.

Specimens of serum from each one of the normal horses used in this work appear in the above series of guinea pigs, which serve as controls.

Donkey serum is also harmless for normal guinea pigs and is just as toxic as horse serum to a sensitized guinea pig.

Uhlenhuth (Zur Kenntniss der giftigen Eigenschaften des Blutserums, Ztschr. f. Hyg., v. 26, 1897, p. 384) found that normal horse serum, when injected intravenously into rabbits, is harmless. He injected as large quantities as 60 c. c. per 1 kilogram of rabbit and found that this caused no reaction at all. On the other hand he found that 11 c. c. of sheep serum, 12 c. c. of hog serum, or 6 c. c. of cattle serum per 1 kilogram of rabbit, when injected intravenously, caused the death of the animal.

The nontoxic action of horse serum on animals was further shown by Hermann Pfeiffer (Ueber die nekrotisirende Wirkung normaler

^aG. P., abbreviation for guinea pig. The numbers refer to the laboratory serial numbers.

Seren, *Ztschr. f. Hyg. u. Infektionskrankh.*, v. 51, (2), pp. 181-196, 1905), who first confirmed the above work of Uhlenhuth and then showed that the subcutaneous inoculation of large quantities of horse serum into guinea pigs produced at most a slight local reaction. He found on the other hand that the serum of certain other animals, e. g., cattle, hog, man, when injected subcutaneously into guinea pigs, produced a local reaction and in large quantities caused necrosis.

We took the temperature of a number of guinea pigs twice daily for eighteen days following the injection of large quantities of horse serum subcutaneously, in order to determine whether a febrile reaction followed. No marked deviation from the normal temperature was noted.

ACTION OF ANTITOXIC HORSE SERUM UPON NORMAL GUINEA PIGS.

It is a well-known fact that large quantities of horse serum containing high antitoxic potency may be injected subcutaneously or into the peritoneal cavity of a normal guinea pig without causing symptoms. We use this method of testing the diphtheria antitoxin bought upon the open market to determine its freedom from bacterial and toxic impurities. Of the many guinea pigs thus inoculated none has shown untoward effects except in the case of bacterial or toxic contaminations. This method of testing the purity of antitoxin is also used by the manufacturers almost daily. We may therefore state that diphtheria antitoxic serum when injected into a normal guinea pig causes no symptoms.

However, we present the following experimental data, which serve as controls for this work, because the normal guinea pigs in the following series have been inoculated into the peritoneal cavity with large quantities of the antitoxic horse serums subsequently used in this work.

- G. P. No. 300. Six c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. No symptoms.
- G. P. No. 301. Do.
- G. P. No. 302. Six c. c. antitoxic horse serum (Natl. V. 14) injected into the peritoneal cavity. No symptoms.
- G. P. No. 303. Do.
- G. P. No. 304. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. No symptoms.
- G. P. No. 305. Do.
- G. P. No. 306. Six c. c. antitoxic horse serum (NYBH 10B, Gibson) injected into the peritoneal cavity. No symptoms.
- G. P. No. 307. Six c. c. antitoxic horse serum (NYBH 13C, Gibson) injected into the peritoneal cavity. No symptoms.
- G. P. No. 308. Six c. c. antitoxic horse serum (Alex. A 211) injected into the peritoneal cavity. No symptoms.
- G. P. No. 309. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.
- G. P. No. 310. Do.

Part II.

HORSE SERUM IS POISONOUS TO A "TREATED" OR "USED" GUINEA PIG.

It has long been known by some of the manufacturers of diphtheria antitoxin that when antidiphtheric serum is inoculated into a used guinea pig the result is almost invariably death. By a "used" or "treated" guinea pig we mean one that has recovered from the effects of an inoculation of the toxine-antitoxin mixture used in testing the potency of diphtheria antitoxin. For example:

G. P. No. 4191. Six c. c. antitoxic horse serum (Alex. 192) injected into the peritoneal cavity. Death in 15 minutes.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. $5 + \frac{1}{380}$ c. c. antitoxic horse serum (PD&Co 08033).]

G. P. No. 4103. Nine c. c. antitoxic horse serum (Alex. 193) injected into the peritoneal cavity. Dead in 5 minutes.

[Previous treatment: 31 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + \frac{1}{200}$ c. c. antitoxic horse serum (Alex. 190).]

G. P. No. 4330. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into peritoneal cavity. Dead in 2 minutes.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. $5 + \frac{1}{200}$ c. c. antitoxic horse serum (Alex. 185).]

G. P. No. 6B. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into peritoneal cavity. Dead in 27 minutes.

[Previous treatment: 86 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + 1$ unit antitoxic horse serum (Standard B25).]

G. P. No. 4381. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 10 minutes.

[Previous treatment: 11 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + \frac{1}{310}$ c. c. antitoxic horse serum (Natl. V. 10).]

G. P. No. 4336. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 12 minutes.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. $5 + \frac{1}{380}$ c. c. antitoxic horse serum (PD&Co 07635).]

G. P. No. 4369. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + \frac{1}{400}$ antitoxic horse serum (Cutter 1461).]

G. P. No. 4377. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + \frac{1}{300}$ c. c. antitoxic horse serum (Natl. V. 7).]

- G. P. No. 4526. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 30 minutes.
[Previous treatment: 17 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 4491. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 41 minutes.
[Previous treatment: 18 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 4494. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 37 minutes.
[Previous treatment: 19 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 75. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 3 hours.
[Previous treatment: 15 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. IX. 17).]
- G. P. No. 88. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 15 days prior, inoculated subcutaneously with 0.006 c. c. toxine No. 7+1 unit antitoxic horse serum (Natl. IX. 17).]
- G. P. No. 4522. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 20 minutes.
[Previous treatment: 20 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 4500. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 21 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 4471. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 8 minutes.
[Previous treatment: 22 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. IX. 17).]
- G. P. No. 4503. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.^a
[Previous treatment: 22 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 4499. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 20 minutes.
[Previous treatment: 24 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]
- G. P. No. 4465. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 40 minutes.
[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. VIII. 17).]
- G. P. No. 4387. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 28 days prior, inoculated subcutaneously with 0.2 c. c. toxine No. 58+1 unit antitoxic horse serum (Standard B27).]

^a Explanation of occasional irregularities, page 63.

G. P. No. 4509. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 25 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

G. P. No. 143. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Dead in 35 minutes.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns 1351).]

G. P. No. 73. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 57 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+250 units antitoxic horse serum (Natl. IX. 17).]

G. P. No. 82. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 57 days prior, inoculated subcutaneously with 0.006 c. c. toxine No. 7+ $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. IX. 17).]

G. P. No. 139. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Dead in 15 minutes.

[Previous treatment: 49 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns 1351).]

All of the above pigs were first given the toxine-antitoxin mixtures in order to test the strength of diphtheria antitoxic serum bought on the open market in accordance with the law of July 1, 1902.

Horse serum is also toxic when injected subcutaneously and in small quantities, as will be seen from the following experiments:

G. P. No. 4951. Six c. c. normal horse serum (roan) inoculated subcutaneously. Dead in 35 minutes.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{350}$ c. c. antitoxic horse serum (NYBH 10B).]

G. P. No. 5047. Same injection. Dead in 40 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{400}$ c. c. antitoxic horse serum (Alex. A205).]

G. P. No. 4950. Same injection. Symptoms; recovered.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{300}$ c. c. antitoxic horse serum (NYBH 10B).]

G. P. No. 5046. Same injection. Dead in 40 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{400}$ c. c. antitoxic horse serum (Alex. A204).]

G. P. No. 4524. Six c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{350}$ c. c. antitoxic horse serum (Alex. 192).]

G. P. No. 4623. One c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{300}$ c. c. antitoxic horse serum (Alex. 192).]

G. P. No. 4512. One c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Dead in 81 minutes.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

G. P. No. 4502. Six c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

G. P. No. 4514. Two-tenths c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

SYMPTOMS CAUSED BY THE INJECTION OF HORSE SERUM INTO A SUSCEPTIBLE GUINEA PIG.

Very characteristic symptoms are produced by horse serum, either normal or antitoxic, when injected into a susceptible guinea pig. The symptoms are apparently the same whether the injection is made subcutaneously or into the peritoneum, or whether normal or antitoxic horse serum is used. In five or ten minutes after injection the pig manifests indications of respiratory embarrassment by scratching at the mouth, coughing, and sometimes by spasmodic, rapid, or irregular breathing; the pig becomes restless and agitated. This stage of exhilaration is soon followed by one of paresis or complete paralysis. The pig is unable to stand or, if it attempts to move, falls upon its side; when taken up it is limp. Spasmodic, jerky, and convulsive movements now supervene.

Pigs in this stage with complete paralysis may fully recover, but usually convulsions appear, and are almost invariably a forerunner of death. Symptoms appear about ten minutes after the injection has been given; occasionally in pigs not very susceptible they are delayed thirty to forty-five minutes. Only in one or two instances of the several hundred pigs which we have observed have the symptoms developed after one hour. Pigs developing symptoms as late as this are not very susceptible and do not die. The chain of symptoms is exceedingly characteristic. The symptoms do not always follow in the order given. Death usually occurs within an hour and frequently in less than thirty minutes.

THE POISONOUS ACTION OF HORSE SERUM ACTS UPON THE RESPIRATORY CENTERS.

Judging from the symptoms produced by the injection of horse serum into a susceptible guinea pig we assumed that the poison acted upon the nervous system. Autopsies done immediately after the death of the guinea pigs showed invariably that the heart continued to beat long after respiration had ceased. In some instances the heart would continue to beat a full hour when exposed. This would seem to indicate that we were dealing with a poison which caused death through the nervous control of the respiration, and the following experiment shows that this effect is certainly not local.

G. P. No. 4526. Six c. c. antitoxic horse serum (National VIII. 17) were injected into the peritoneal cavity. Death in 30 minutes.

[Previous treatment: 17 days prior, inoculated subcutaneously with 0.19 c. c. of toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

Immediately after death the phrenic nerve was exposed and stimulated high up, causing contractions of the diaphragm both upon making and breaking the galvanic current. The contractions were also caused with the induced current. The contractions of the diaphragm caused by stimulating the phrenic nerve in this way were produced with a weaker current than those required to cause similar contractions in a normal control guinea pig.

Part III.

THE TOXIC ACTION BEARS NO RELATION TO DIPHTHERIA.

THE POISON IS NOT TOXONE.

It occurred to us that possibly diphtheria antitoxic serum may contain free toxone which, when injected into a "used" or "treated" guinea pig, might produce acute effects upon the nervous system of such a pig, which, on account of the previous effects of diphtheria toxine, had been rendered peculiarly susceptible. It is well known that the toxone does not cause the acute death of a guinea pig, but only produces a local edema and late paralysis. This fact, first demonstrated by Ehrlich, may readily be demonstrated by inoculating guinea pigs with toxine and antitoxin mixed in such proportions so that the toxine is but partly neutralized. We were further led to believe that the poisonous effects of horse serum upon a treated guinea pig might be a manifestation of the toxones because the symptoms so plainly point to the nervous system. The pigs almost invariably show paresis or paralysis.

The fact that neither toxone nor any other constituent in the toxine plays any rôle in the poisonous action of horse serum is demonstrated in the following experiment:

G. P. No. 4161. 0.1 c. c. toxine No. 15 (MLD=.01) was injected into the peritoneal cavity. No symptoms. Completely paralyzed at the time, resulting from previous treatment.

[Previous treatment: 31 days previously inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{20}$ c. c. diphtheria antitoxic serum (Mulford's No. 942).]

One hour 50 min. later this same pig was inoculated with 6 c. c. diphtheria antitoxic serum (P. D. & Co. No. 08022) into the peritoneal cavity. Death in 10 minutes.

It is well known that overpowering doses of toxine injected either subcutaneously or into the peritoneal cavity of a guinea pig require about twenty hours to kill the animal. These large doses of toxine do not cause immediate symptoms.

It occurred to us, however, that while toxine alone may not have this power, nevertheless when it is mixed with antitoxic horse serum and when large doses of the mixture are injected into a guinea pig there may be a sufficient liberation of toxone or other poisonous substances capable of producing symptoms and sudden death.

The following mixture of toxine and antitoxin represents these two substances in the proportion of the L^o dose:

G. P. 4483. 1.6 c. c. toxine No. 7+11.5 units antitoxic serum (standard B27) injected subcutaneously. No symptoms.

18 days later 6 c. c. antitoxic horse serum (National VIII, 17) injected into the peritoneal cavity of the same pig. Death 30 minutes.

In a similar way the effects of mixing large doses of the diphtheria toxine with normal horse serum were tested, as follows:

G. P. No. 40. Six c. c. normal horse serum (roan horse)+0.3 c. c. diphtheria toxine No. 5 mixed in vitro and injected into the peritoneal cavity. No immediate symptoms. Died 2 days later.

GUINEA PIGS CAN NOT BE RENDERED SUSCEPTIBLE BY PRIOR INFECTIONS WITH
THE BACILLUS DIPHThERIEÆ.

When this work was first undertaken it was thought to have a bearing upon sudden deaths in children suffering with diphtheria. The work was begun in order to discover, if possible, the cause of this accident. We thought that possibly by injecting small quantities of a virulent culture of the Klebs-Löffler bacillus into guinea pigs, in that way imitating mild cases of diphtheria, some of these pigs could be rendered susceptible to subsequent inoculations of antitoxic horse serum. This, however, is not the case for guinea pigs, as is plainly seen in the following experiments, in which a number of guinea pigs were treated with sufficient quantities of a culture of the Klebs-Löffler bacillus to cause slight symptoms and at varying intervals of time were inoculated again into the peritoneal cavity with large quantities of antitoxic horse serum. In no instance did the guinea pigs show any ill effects from this latter treatment.

G. P. No. 41. Six c. c. antitoxic horse serum (Natl. VIII, 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 4 days prior, inoculated subcutaneously with 0.1 c. c. suspension.]

G. P. No 9. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: 7 days prior, inoculated subcutaneously with 1 gtt. of 24-hour suspension.]

G. P. No. 51. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: 7 days prior, inoculated subcutaneously with 0.1 c. c. of suspension.]

G. P. No. 42. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: 9 days prior, inoculated subcutaneously with 1 gtt. 24-hour suspension.]

G. P. No. 56. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: 9 days prior, inoculated subcutaneously with 0.1 c. c. suspension.]

G. P. No. 43. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: 12 days prior, inoculated subcutaneously with 1 gtt. 24-hour suspension.]

G. P. No. 45. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: 14 days prior, inoculated subcutaneously with 1 gtt. 24-hour suspension.]

G. P. No. 58. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: *21 days prior*, inoculated subcutaneously with 0.1 c. c. suspension.]

G. P. No. 44. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: *24 days prior*, inoculated subcutaneously with 1 gtt. 24-hour suspension.]

G. P. No. 52. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: *27 days prior*, inoculated subcutaneously with 0.1 c. c. 24-hour suspension.]

G. P. No. 50. Six c. c. same serum and injection as g. p. 41. No symptoms.

[Previous treatment: *32 days prior*, inoculated subcutaneously with 1 gtt. 24-hour suspension.]

DIPHTHERIA TOXINE CAN NOT RENDER GUINEA PIGS SUSCEPTIBLE.

For the same reason that guinea pigs were treated with cultures of the *Bacillus diphtheriæ* we also attempted to render them susceptible by the injection of small quantities of diphtheria toxine. On account of the great importance of this subject a large number of guinea pigs were used to demonstrate the rôle which the diphtheria toxine may play in the subsequent action of horse serum. Our experiments demonstrate conclusively that diphtheria toxine alone plays absolutely no rôle in rendering guinea pigs susceptible to the toxic action of horse serum; for in no instance, as will be seen in the following series, does the guinea pig show the slightest effects when subsequently injected with large quantities of serum.

G. P. No. 4584. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: *2 days prior*, inoculated subcutaneously with 0.001 c. c. toxine No. 7.]

G. P. No. 4593. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *3 days prior*, as g. p. 4584.]

G. P. No. 4534. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *4 days prior*, inoculated subcutaneously with 0.002 c. c. toxine No. 7.]

G. P. No. 4550. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *5 days prior*, as g. p. 4534.]

G. P. No. 4548. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *6 days prior*, as g. p. 4534.]

G. P. No. 4585. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *6 days prior*, as g. p. 4584.]

G. P. No. 4432. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *7 days prior*, as g. p. 4534.]

G. P. No. 4434. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *7 days prior*, inoculated subcutaneously with 0.004 c. c. toxine No. 7.]

G. P. No. 4426. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *8 days prior*, as g. p. 4534.]

G. P. No. 4583. Six c. c. same serum and injection as g. p. 4584. No symptoms.

[Previous treatment: *9 days prior*, as g. p. 4534.]

- G. P. No. 4579. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *10 days prior*, as g. p. 4534.]
- G. P. No. 4582. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *11 days prior*, as g. p. 4534.]
- G. P. No. 4430. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *12 days prior*, as g. p. 4534.]
- G. P. No. 4572. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *12 days prior*, as g. p. 4534.]
- G. P. No. 4568. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *13 days prior*, as g. p. 4534.]
- G. P. No. 4576. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *14 days prior*, as g. p. 4534.]
- G. P. No. 4577. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *16 days prior*, as g. p. 4534.]
- G. P. No. 4535. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *17 days prior*, as g. p. 4534.]
- G. P. No. 4547. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *18 days prior*, as g. p. 4534.]
- G. P. No. 4580. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *19 days prior*, as g. p. 4534.]
- G. P. No. 4556. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *20 days prior*, as g. p. 4534.]
- G. P. No. 4558. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *21 days prior*, as g. p. 4534.]
- G. P. No. 4545. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *23 days prior*, as g. p. 4534.]
- G. P. No. 4555. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *24 days prior*, as g. p. 4534.]
- G. P. No. 4541. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *26 days prior*, as g. p. 4534.]
- G. P. No. 4404. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *27 days prior*, inoculated subcutaneously with 0.002 c. c. toxine No. 5.]
- G. P. No. 4454. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *27 days prior*, inoculated subcutaneously with 0.01 c. c. toxine No. 19.]
- G. P. No. 4565. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *27 days prior*, as g. p. 4534.]
- G. P. No. 4554. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *30 days prior*, as g. p. 4534.]
- G. P. No. 4578. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *31 days prior*, as g. p. 4534.]
- G. P. No. 4542. Six c. c. same serum and injection as g. p. 4584. No symptoms.
[Previous treatment: *33 days prior*, as g. p. 4534.]
- G. P. No. 4529. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. No symptoms.
[Previous treatment: *46 days prior*, as g. p. 4534.]
- G. P. No. 4428. Do.
- G. P. No. 4427. Do.
- G. P. No. 4431. Do.

G. P. No. 4567. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 65 days prior, as g. p. 4534.]

G. P. No. 4554. Do.

G. P. No. 4553. Do.

DIPHTHERIA ANTITOXIN PLAYS NO RÔLE IN THIS ACTION.

Before we realized that the diphtheria toxine or antitoxin played no rôle in rendering guinea pigs susceptible to subsequent injections of horse serum we prepared the following series of guinea pigs, in order to eliminate the antitoxin as a factor. These pigs were injected subcutaneously with a mixture of 1 c. c. of normal horse serum and a small quantity of diphtheria toxine, slightly less than a minimal lethal dose. This was done for comparison with the susceptibility produced by the toxine-antitoxin mixtures.

G. P. No. 91. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms. Died 12 hours later.

[Previous treatment: 65 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7+1 c. c. normal horse serum (Sam).]

G. P. No. 296. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 60 minutes.

[Previous treatment: 71 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7+1 c. c. normal horse serum (Sam).]

G. P. No. 96. Do. Dead in 40 minutes.

G. P. No. 93. Do. Symptoms; recovered.

G. P. No. 90. Do.

It will be seen from our experiments that guinea pigs are quite as sensitive when previously treated with toxine-normal serum as with the toxine-antitoxin mixtures.

In order to compare the toxic action of normal serum with antitoxic serum upon pigs so treated, four animals of the above series were inoculated with antitoxic horse serum, as follows:

G. P. No. 92. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms. Died 12 hours later.

[Previous treatment: 15 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7+1 c. c. normal horse serum (Sam).]

G. P. No. 98. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Dead in 53 minutes.

[Previous treatment: 58 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7+1 c. c. normal horse serum (Sam).]

G. P. No. 95. Do. Dead in 43 minutes.

G. P. No. 94. Same injection. Symptoms; recovered.

[Previous treatment: 65 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7+1 c. c. normal horse serum (Sam).]

It is evident from the above that fresh normal serum is quite as poisonous to a sensitized guinea pig as is antitoxic horse serum.

In order further to eliminate the antitoxin as a factor in this problem, the following series of used or treated guinea pigs were injected with normal horse serum:

G. P. No. 4100. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 15 minutes.

[Previous treatment: 36 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{250}$ c. c. antitoxic horse serum (Alex. 190).]

G. P. No. 4105. Same injection. Dead in 30 minutes.

[Previous treatment: 36 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Alex. 189).]

G. P. No. 4106. Same injection. Dead in 5 minutes.

[Previous treatment: 36 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Alex. 189).]

G. P. No. 4331. Same injection. Dead in 90 minutes.

[Previous treatment: 25 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{250}$ c. c. antitoxic horse serum (Alex. 185).]

G. P. No. 4351. Same injection. Dead in 40 minutes.

[Previous treatment: 18 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{400}$ c. c. antitoxic horse serum (PD&Co 08021).]

G. P. No. 3950. Six c. c. normal horse serum (Sam) injected into peritoneal cavity. Dead in 10 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{280}$ c. c. antitoxic horse serum (Hubbert 1).]

G. P. No. 3951. Six c. c. normal horse serum (Jane) injected into the peritoneal cavity. Dead in 30 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{290}$ c. c. antitoxic horse serum (Hubbert 1).]

G. P. No. 3952. Six c. c. normal horse serum (Sp.) injected into the peritoneal cavity. Dead in 38 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{290}$ c. c. antitoxic horse serum (Hubbert 1).]

G. P. No. 3953. Six c. c. normal donkey serum (No. 58) injected into the peritoneal cavity. Dead in 60 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{310}$ c. c. antitoxic horse serum (Hubbert 1).]

G. P. No. 4109. One c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 37 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{440}$ c. c. antitoxic horse serum (Alex. 188).]

G. P. No. 4945. Six c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 34 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{420}$ c. c. antitoxic horse serum (Wellcome 478).]

G. P. No. 4934. Six c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 34 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{350}$ c. c. antitoxic horse serum (Wellcome 479).]

G. P. No. 4930. Six c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 34 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{300}$ c. c. antitoxic horse serum (Wellcome 475).]

G. P. No. 4931. Six c. c. normal horse serum (roan) inoculated subcutaneously. Dead in 5 minutes.

[Previous treatment: 34 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{370}$ c. c. antitoxic horse serum (Wellcome 475).]

G. P. No. 4941. Six c. c. normal horse serum (roan) inoculated subcutaneously. Dead in 20 minutes.

[Previous treatment: 34 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{700}$ c. c. antitoxic horse serum (Wellcome 474).]

All of the above animals and most of those which appear upon the subsequent pages of this bulletin were first used to test the strength of the diphtheria antitoxin bought on the open market in accordance with the law of July 1, 1902.

The following series of guinea pigs were given small quantities of antitoxic horse serum, some subcutaneously and some intraperitoneally, in order to compare the sensitizing action by these two methods of inoculation. At the second injection they were all given 6 c. c. of normal horse serum into the peritoneal cavity.

G. P. No. 276. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 25 minutes.

[Previous treatment: 17 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. V. 14).]

G. P. No. 277. Do. Dead in 30 minutes.

G. P. No. 278. Do. Dead in 55 minutes.

G. P. No. 279. Do. Symptoms; recovered.

G. P. No. 280. Do. Symptoms; recovered.

G. P. No. 281. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 17 days prior, $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. V. 14) injected into the peritoneal cavity.]

G. P. No. 282. Do. Dead in 23 hours.

G. P. No. 283. Do. Symptoms; recovered.

G. P. No. 284. Do. Dead in 60 minutes.

G. P. No. 285. Do. Symptoms; recovered.

From the above series it will be seen that guinea pigs may be rendered as susceptible by intraperitoneal as by subcutaneous inoculations.

Finally, in order to demonstrate without doubt that neither antitoxin nor diphtheria toxine plays any part in this action, and to show that this action is a property of normal horse serum, we treated a number of guinea pigs giving them at both the first and second injection fresh normal horse serum, with the following results:

G. P. No. 101. Three c. c. normal (roan) horse serum injected into the peritoneal cavity. Dead in 35 minutes.

[Previous treatment: 55 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. normal horse serum (Jane).]

G. P. No. 105. One c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: As above.]

G. P. No. 104. One c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: As above.]

G. P. No. 102. Three c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: As above.]

G. P. No. 286. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 25 minutes.

[Previous treatment: 17 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. normal horse serum (roan).]

G. P. No. 287. Do. Dead in 50 minutes.

G. P. No. 288. Do. Symptoms; recovered.

G. P. No. 289. Do. do do

G. P. No. 290. Do. do do

Part IV.

THE TOXIC PRINCIPLE.

At one time we made efforts to isolate the active principle in horse serum which causes the symptoms, but as soon as we realized that the toxic principle present in horse serum exerts its action in quantities so minute as to place it almost in the category of the ferments, and, further, when we concluded from our work that this toxic principle is doubtless one of those highly organized and complex proteid substances belonging to the "haptin" group, we recognized how hopeless it would be with present technique to isolate this substance. Nevertheless, we devoted much time and study to the relation of this toxic principle to various chemical, physical, and electrical influences. The practical importance of eliminating or neutralizing this toxic principle from horse serum is at once evident.

IS THE POISON SPECIFIC?

Whether the poisonous substance in horse serum is specific may be determined in several ways. We first endeavored to determine whether guinea pigs treated with horse serum are susceptible to the serums of other animals; and, secondly, whether guinea pigs treated with the serums of other animals are susceptible to subsequent injections of horse serum.

The following is a list of animals treated with horse serum and subsequently tested with the blood serums of other animals.

It will be noticed that in this list some of the guinea pigs were treated with donkey serum instead of horse serum, but as the donkey serum in our hands has shown itself to act the same as horse serum we have used them interchangeably.

Table showing the effect of alien serums upon guinea pigs sensitized with horse serum.

No. of guinea pig.	Kind and amount of normal serum.	Previous treatment.		Result.
		Days prior.	Inoculated subcutaneously with—	
178	Cattle, 6 c. c.	34	$\frac{1}{250}$ c. c. donkey serum.....	Symptoms, recovered.
149do.....	41	0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns 1351).	Do.
180	Hog, 6 c. c.	34	$\frac{1}{250}$ c. c. donkey serum.....	No symptoms.
138do.....	41	0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns 1351).	Symptoms, recovered.
4743	Hog, 1 c. c.	41	0.139 c. c. toxine No. 5 + $\frac{1}{350}$ c. c. horse serum (Alex. 192).	Do.
179	Sheep, 6 c. c.	34	$\frac{1}{250}$ c. c. donkey serum.....	Do.
152do.....	41	0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns 1351).	Do.
177	Cat, 6 c. c.	34	$\frac{1}{250}$ c. c. donkey serum.....	Do.
124do.....	41	0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns 1351).	No symptoms.
4744	Cat, 1 c. c.	41	0.139 c. c. toxine No. 5 + $\frac{1}{350}$ c. c. horse serum (Alex. 192).	Symptoms, recovered.
121	Rabbit, 6 c. c.	41	0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns 1351).	Do.
4380do.....	19	0.22 c. c. toxine No. 7 + $\frac{1}{250}$ c. c. horse serum (Natl. V. 10).	Do.
4374do.....	19	0.22 c. c. toxine No. 7 + $\frac{1}{250}$ c. c. horse serum (Natl. V. 7).	Do.
153	Dog, 6 c. c.	41	0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns 1351).	Do.
4379do.....	19	0.22 c. c. toxine No. 7 + $\frac{1}{250}$ c. c. horse serum (Natl. V. 10).	Do.
4742	Dog, 1 c. c.	41	0.139 c. c. toxine No. 7 + $\frac{1}{350}$ c. c. horse serum (Alex. 192).	Do.
4375	Guinea pig, 3 c. c. ...	19	0.22 c. c. toxine No. 7 + $\frac{1}{250}$ c. c. horse serum (Natl. V. 7).	No symptoms.

As the above series of guinea pigs previously treated with horse serum showed unmistakable susceptibility to subsequent injections of the blood serum of other animals, we are justified in saying that the action is not specific; but there is a very evident quantitative difference. It will be noticed that none of these guinea pigs died, and it was a matter of observation that, for the most part, they had characteristic but mild symptoms.

We next took up the question as to whether a guinea pig may be sensitized to horse serum with the blood serum of animals other than the horse. The following is a list of guinea pigs which had been treated by the subcutaneous inoculation of small quantities ($\frac{1}{250}$ c. c.) of blood serum from the rabbit, rat, donkey, cat, dog, hog, sheep, chicken, cattle, and man. Each pig was subsequently injected with 6 c. c. of antitoxic horse serum (Natl. IX. 17) into the peritoneal cavity.

Table showing the results of injecting 6 c.c. of antitoxic horse serum (Natl. IX. 17) into the peritoneal cavity of guinea pigs treated from 25 to 34 days prior with $2\frac{1}{50}$ c. c. of the blood serum of other animals.

No. of guinea pig.	Previous treatment.		Result.
	Kind of serum.	Days prior.	
171	Rabbit..... $2\frac{1}{50}$ c. c.	25	No symptoms.
172do.....do.....	34	Do.
174do.....do.....	34	Symptoms, recovered.
167	Rat.....do.....	25	No symptoms.
168do.....do.....	34	Do.
169do.....do.....	34	Do.
170do.....do.....	34	Do.
176	Donkey.....do.....	25	Do.
191	Cat.....do.....	25	Do.
192do.....do.....	34	Symptoms, recovered.
193do.....do.....	34	Symptoms (?), recovered.
214	Dog.....do.....	26	No symptoms.
215do.....do.....	35	Do.
212do.....do.....	35	Symptoms, recovered.
185	Hog.....do.....	30	No symptoms.
186do.....do.....	30	Symptoms, recovered.
182	Sheep.....do.....	30	Do.
184do.....do.....	30	No symptoms.
196	Chicken.....do.....	26	Symptoms, recovered.
197do.....do.....	26	Do.
206	Cattle.....do.....	31	No symptoms.
207do.....do.....	31	Do.
210do.....do.....	31	Do.
201	Man.....do.....	31	Symptoms, recovered.
202do.....do.....	31	No symptoms.

As the above series of guinea pigs was tested with antitoxic horse serum, we tested another series, similarly sensitized, with normal horse serum, as shown in the table on the following page, the results in all respects being similar.

Table showing the results of injecting $\frac{1}{4}$ c. c. of normal horse serum (roan) into the peritoneal cavity of guinea pigs from 47 to 56 days prior with $\frac{1}{250}$ c. c. of the blood serum of other animals.

No. of guinea pig.	Previous treatment.		Result.
	Kind of serum.	Days prior.	
173	Rabbit..... $\frac{1}{250}$ c. c..	55	Symptoms, recovered.
175do.....do.....	55	Do.
195	Cat.....do.....	55	Do.
213	Dog.....do.....	56	Do.
211do.....do.....	56	Do.
187	Hog.....do.....	51	Do.
189do.....do.....	51	Do.
190	Sheep.....do.....	47	No symptoms.
183do.....do.....	51	Symptoms, recovered.
181do.....do.....	51	Do.
199	Chicken.....do.....	47	No symptoms.
198do.....do.....	47	Symptoms (?), recovered.
200do.....do.....	47	Symptoms, recovered.
203	Man.....do.....	52	No symptoms.
204do.....do.....	52	Symptoms, recovered.
205do.....do.....	52	Do.

We think it is plain from the above that this action is not strictly specific for horse serum; that is, guinea pigs treated with horse serum are rendered somewhat susceptible to the subsequent injection of the serum of certain other species and that guinea pigs treated with the serum of other animals are slightly sensitive to the toxic action of horse serum. However, it is also perfectly plain from this series of experiments that the action is quantitatively specific, for it will be noticed that of the many guinea pigs sensitized with the blood serum of animals other than the horse, none died from subsequent injections of large quantities (6 c. c.) of horse serum. The same may be said of the action of these other serums upon guinea pigs previously treated with horse serum. While most of these serums produced symptoms, none of the guinea pigs died.

In other words, there is plainly a distinct quantitative difference, both in the results of the power of horse serum to render guinea pigs susceptible to other serums and in its toxic action upon guinea pigs sensitized by other serums.

The action of horse serum upon other animals than the guinea pig is treated of in another chapter (p. 55).

ARE OTHER BLOOD SERUMS EQUALLY TOXIC?

We now know that guinea pigs previously treated with small injections of horse serum become very susceptible to subsequent injections of horse serum, but only slightly susceptible to the blood serum of other animals. It becomes important to determine whether

guinea pigs treated with the serum of other animals (dog, hog, rat, cattle, sheep, cat) become as highly sensitized to a second injection of the homologous serum.

The following series of guinea pigs were all sensitized with 1/250 c. c. of the blood of various animals. Subsequently they were injected with horse serum to which they either did not respond or, after characteristic symptoms, recovered. These guinea pigs were finally injected with large quantities of the same kind of serum as that used at the first injection.

Dog serum.

G. P. No. 214. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 26 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *dog* serum.]

5 hrs. later 6 c. c. *dog* serum injected into the peritoneal cavity. Symptoms.

G. P. No. 215. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 35 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *dog* serum.]

22 days later 6 c. c. *dog* serum injected into peritoneal cavity. Severe symptoms.

G. P. No. 212. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. Mild symptoms.

[Previous treatment: 35 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *dog* serum.]

22 days later 6 c. c. *dog* serum injected into peritoneal cavity. Severe symptoms.

G. P. No. 211. Four c. c. normal *horse* serum (roan) injected into the peritoneal cavity. Symptoms.

[Previous treatment: 56 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *dog* serum.]

1 day later 6 c. c. *dog* serum injected into the peritoneal cavity. Dead in 35 minutes

Hog serum.

G. P. No. 186. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. Severe symptoms.

[Previous treatment: 30 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *hog* serum.]

22 days later 6 c. c. *hog* serum injected into the peritoneal cavity. Severe symptoms.

G. P. No. 185. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 30 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *hog* serum.]

22 days later 5 c. c. *hog* serum injected into the peritoneal cavity. No symptoms.

G. P. No. 187. Four c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 51 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *hog* serum.]

1 day later 6 c. c. *hog* serum injected into the peritoneal cavity. Symptoms.

G. P. No. 189. Same injection and previous treatment. No symptoms.

1 day later 6 c. c. *hog* serum injected into the peritoneal cavity. Symptoms.

Cattle serum.

G. P. No. 206. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 31 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *cattle* serum.]

22 days later 6 c. c. *cattle* serum injected into the peritoneal cavity. Dead in 120 minutes.

G. P. No. 210. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 31 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *cattle* serum.]

22 days later 6 c. c. *cattle* serum injected into the peritoneal cavity. Dead in 45 minutes.

G. P. No. 207. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 31 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *cattle* serum.]

22 days later 6 c. c. *cattle* serum injected into the peritoneal cavity. Dead in 90 minutes.

Sheep serum.

G. P. No. 184. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 30 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *sheep* serum.]

22 days later 6 c. c. *sheep* serum injected into the peritoneal cavity. Severe symptoms; dead in 23 hours.

G. P. No. 182. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. Severe symptoms.

[Previous treatment: 30 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *sheep* serum.]

22 days later 6 c. c. *sheep* serum injected into the peritoneal cavity. Severe symptoms.

G. P. No. 190. Four c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 47 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *sheep* serum.]

1 day later 6 c. c. *sheep* serum injected into the peritoneal cavity. Severe symptoms.

G. P. No. 183. Four c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms.

[Previous treatment: 51 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *sheep* serum.]

1 day later 6 c. c. *sheep* serum injected into the peritoneal cavity. Dead in 18 hours.

G. P. No. 181. Same injection and previous treatment. Mild symptoms.

1 day later 6 c. c. *sheep* serum injected into the peritoneal cavity. Severe symptoms. Dead in 21 hours.

• *Cat serum.*

G. P. No. 192. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. Severe symptoms.

[Previous treatment: 34 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *cat* serum.]

22 days later 6 c. c. *cat* serum injected into the peritoneal cavity. Severe symptoms.

G. P. No. 195. Four c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms.

[Previous treatment: 55 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. *cat* serum.]

1 day later 6 c. c. *cat* serum injected into the peritoneal cavity. Dead in 35 minutes.

Rat serum.

G. P. No. 168. Six c. c. antitoxic *horse* serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 34 days prior inoculated subcutaneously with $\frac{1}{250}$ c. c. *rat* serum.]

2 hours later 2 c. c. *rat* serum injected into the peritoneal cavity. Severe symptoms. Dead in 3 hours.

We infer from the above series that guinea pigs treated with the serums of various animals and subsequently injected are much more susceptible to homologous serums than to heterologous serums. We have here another indication that this toxic action of blood serum is quantitatively specific.

We expect to take up the work with the serums of other animals more in detail, and the results will be reported at another time.

THE RELATION OF HEMOLYSIS.

So much work has recently been done indicating that the toxic property of blood serum is closely allied with its hemolytic action that we made some experiments in order to determine what connection exists between the hemolytic and toxic action of horse serum upon guinea pigs. As a result of these studies we believe that we have shown very clearly that blood serum may contain an acute poison entirely independent of any hemolytic action.

Landois ^a in his work on transfusion showed long ago (1875) that the blood serum of many mammals dissolves the red blood cells of other mammals. Landois specifically demonstrated that the red blood corpuscles of rabbits, when mixed with alien blood serum, are readily dissolved, while, on the other hand, the red blood corpuscles of cats and dogs are much more resistant. If large quantities of red blood corpuscles are dissolved, there follows an excretion of hemoglobin through the kidneys, intestines, and also into the serous cavities. If the serum is injected into the blood stream of a rabbit, some of the erythrocytes of the rabbit are dissolved in vivo, as may readily be confirmed microscopically; but before the corpuscles are dissolved there is an agglutination of the blood corpuscles into clumps, by means of which large capillary areas may become plugged. The same process is seen by the further extraction of hemoglobin from the mass of the stroma of the corpuscles which fills the capil-

^a Landois: Lehrbuch der Physiologie des Menschen, 1896. Die Transfusion des Blutes. Leipzig, 1875.

laries. The dissolved hemoglobin now causes further blocking of the vessels by means of clots, which are formed through the action of the hemoglobin upon the leucocytes, freeing the fibrin ferment. From this somewhat complicated process there may result serious symptoms, as dyspnea, convulsions, etc., in proportion to the amount of blood injected. If the amount of blood is large, death may follow, as Landois has shown, with phenomena of asphyxiation. (Uhlenhuth: *Zur Kenntniss der giftigen Eigenschaften des Blutserums. Zeit. f. Hyg.*, vol. 26, 1897, p. 384.)

Hermann Pfeiffer,^a confirming the work of Uhlenhuth upon the necrotic action of blood serums when injected subcutaneously into guinea pigs, believes that the toxic substance producing the necrosis is the same as the hemolytic agent found in the blood serum.

In recent years hemolysis has been studied more particularly by Ehrlich, Morgenroth, Bordet, Metchnikoff, and many others. Much of the work done appears to corroborate the early observations of Landois, who believed that the toxic action of blood serum when injected intravenously depends upon a "globulicidal" action upon the red blood cells and the plugging of the capillaries. On the other hand, we have the views of other authors based in part upon experimental data that the toxic action of blood serum is dependent upon albuminous substances independently of the lytic substance present in the serum.

Creite^b in 1869 was aware of Landois's view concerning hemolysis, but separated the toxic power from the blood serum by means of coagulation (heat).

Also, Weiss^c in 1896 showed by separating albuminous substances from the blood serum by means of heating or absolute alcohol that the serum has no longer the toxic power and concluded, therefore, that the toxic action is brought about by the albumins.

Albu^d separated the albuminous substances from blood serum by precipitation with ammonium sulphate, which he dialyzed out, as it is itself poisonous, and came to the same conclusion as Creite and Weiss.

Rummo^e believed that the toxic substance is a tox-albumin which, according to his views, is formed in the living cells of the respective animals.

^a Hermann Pfeiffer: Über die nekrotisirende Wirkung normaler Seren. *Zeit. f. Hyg.*, 1905, Band 150, p. 183.

^b Creite: Versuche über die Wirkung des Serumweisses nach Injection in das Blut. *Zeit. f. rationelle Med.* Bd. 36, S. 90.

^c Weiss: Ueber die Wirkungen von Blutserum-Injectionen in's Blut. *Pflüger's Arch.*, Bd. 65, 1896.

^d Albu: Untersuchungen über die Toxicität normaler u. pathol. Serumflüssigkeit. *Virchow's Arch.*, Bd. 149, 3.

^e Rummo: Ueber die Giftigkeit des Blutserums bei Menschen und Thieren im normalen Zustande und bei Infectiouskrankheiten. *Wiener med. Woch.*, 1891, nr. 19-20.

Mairet and Bosc ^a were able to distinguish in blood serum a substance capable of producing coagulation and another substance capable of producing poisonous symptoms. They believed both of these substances to be albumins. They were able to eliminate the coagulation-producing substance by heating from 52° to 53° C. or by the addition of sodium chloride and sodium sulphate.

Pearce ^b believes that it appears to be definitely established that red blood corpuscle thrombi occur in the experimental lesions caused by sera possessing hemagglutinative power. He demonstrated that the capillaries of certain areas in the liver are entirely occluded by fused red cells, and he also showed the inability of the products of hemolysis to produce such action and necrotic areas in the liver.

L. Camus and E. Gley ^c first endeavored to separate the hemolytic action from the toxic action of blood serum by means of heating. They found that heat destroys the hemolytic action; but while it diminishes it does not entirely destroy its general toxic action. This work was done with eel serum. In their previous work the two actions seemed about parallel. For instance, eel serum is very hemolytic for rabbits and guinea pigs and equally poisonous for these animals. On the other hand, the red blood cells of the pigeon and those of the porcupine are very resistant to eel serum, and these animals also resist doses which are fatal for the rabbit and the guinea pig. However, these authors finally found an animal, the marmot, for which eel serum had slight hemolytic action but was extremely toxic, and they believed that these researches upon the marmot have permitted them to separate the toxic action of eel serum from its hemolytic action better than did their previous work by means of heating.

We found horse serum to have practically no hemolytic action upon the corpuscles of the guinea pig. This applies with equal force to antitoxic horse serum as to normal horse serum, as may be seen from the following table:

Hemolysis.

G. P. No. 2. Normal pig. Serum obtained by coagulation.

G. P. No. 1. Normal pig. Corpuscles obtained by centrifugation, etc.

^a Mairet and Bosc: Recherches sur les causes de la toxicité du serum du sang. Compt. rend., t. 119, 4, p. 292. Toxicité du serum du sang de l'homme sain., Compt. rend., 1897. Des effets de la chaleur sur la toxicité du sérum. Compt. rend. July 7, 1894.

^b Pearce, Richard M.: A further study of the experimental production of liver necrosis by the injection of hemagglutinative sera. J. M. Research, v. 14, Apr., 1906, p. 541. Pearce, R. M., and Winne, C. K., jr.: Concerning hemagglutins of bacterial origin and their relation to hyalin thrombi and liver necroses. Am. J. M. Sci., v. 128, 1904, p. 669.

^c Camus, L., and Gley, E.: Comparison between the hemolytic and the toxic action of eel's serum in the marmot (*Arctomys marmota*). Arch. internat. de pharmacodyn. et de therapie, tome 15, fasc. 1 and 2, 1905.

G. P. No. 4517. Serum obtained by coagulation.

[Previous treatment: 35 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

G. P. 4510. Corpuscles obtained by centrifugation, etc.

[Previous treatment: 35 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

1 c. c. of—	1 c. c., 5 per cent corpuscles. normal guinea pig No. 1 (washed).		1 c. c., 5 per cent corpuscles. treated guinea pig No. 4510 (washed).	
	Do. +1 gtt. se- rum nor- mal guinea pig No. 2.	Do. +1 gtt. se- rum guinea pig No. 4517.	Do. +1 gtt. se- rum nor- mal guinea pig No. 2.	Do. +1 gtt. se- rum guinea pig No. 4517.
Normal horse serum (Sam.).....	0	0	0	0
Normal donkey serum.....	Faintest trace.	0	0	0
Normal horse serum (Sp.).....	0	Faintest trace.	0	Faintest trace.
Antitoxic horse serum (Natl. VIII. 17)...	0	0	0	0
Antitoxic horse serum (Natl. IX. 19)....	0	0	0	0
Antitoxic horse serum (Natl. V. 14).....	0	0	0	0
Antitoxic horse serum (Alex. A205, Gib- son's method).	Trace.	Trace.	Trace.	Trace.
Salt solution (control).....	0	Trace.	0	0

First the corpuscles were placed in the test tubes, then the various horse serums, and finally the drop of guinea-pig serum.

The corpuscles were obtained by whipping the blood and washing in the usual way four times and suspended so as to make the so-called 5 per cent suspension. After the corpuscles and the serum were mixed they were well shaken and placed in the incubator, again shaken at the end of one hour, again at the end of two hours, and at the end of three hours taken out of the incubator and placed in the ice chest. The readings were taken the next morning.

This work was repeated several times until we were satisfied that neither the normal horse serum nor the antitoxic horse serum had practically any power of dissolving the hemoglobin from the guinea-pig corpuscles. There can therefore be no doubt that there is a toxic substance in the blood serum of horses entirely independent of any hemolytic action. As a further corroboration we may state that autopsies upon guinea pigs which have died from the results of the injections of horse serum showed none of the usual effects, indicating that hemolysis took place within the body.

Further, horse serum heated to 60° for six hours is as toxic as unheated serum.

As a further study of the relation of hemolysis to the toxic action and also of the relation of the toxic principle to the haptin group we made the following experiments:

G. P. No. 249. Four subcutaneous injections of 1.5 c. c. each on successive days, using normal roan horse corpuscles washed three times. The blood serum of this guinea pig developed a high degree of hemolytic power against horse corpuscles. The blood serum of this guinea pig was mixed with equal quantities of normal horse serum and the mixture injected into the following three guinea pigs:

G. P. No. 4993. Two c. c. of the above mixture injected into the peritoneal cavity. Dead in 40 minutes.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{550}$ c. c. antitoxic horse serum (Alex. A206).]

G. P. No. 4988. Same injection. Dead in 30 minutes.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{150}$ c. c. antitoxic horse serum (Alex. A202).]

G. P. No. 4992. Same injection. Dead in 35 minutes.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{500}$ c. c. antitoxic horse serum (Alex. A208).]

The above experiment was repeated as follows:

G. P. No. 248. Four subcutaneous injections of 1.5 c. c. each on successive days were made, using roan corpuscles washed three times. The blood serum of this guinea pig developed a high degree of hemolytic power against horse corpuscles. The serum was mixed with equal quantities of normal horse serum and the mixture injected into the following guinea pigs:

G. P. No. 4913. Four c. c. of the above mixture injected into the peritoneal cavity. Dead in 10 minutes.

[Previous treatment: 41 days prior, inoculated subcutaneously with 0.139 c. c. of toxine No. 5 + $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns 12D).]

G. P. No. 4914. Two c. c. same serum injected into the peritoneal cavity. Dead in 20 minutes.

[Previous treatment: Same as G. P. No. 4913.]

THE RELATION OF PRECIPITIN TO THE TOXIC ACTION.

The precipitins are so specific and so closely related to the cytotoxins that it naturally occurred to us to determine what relation there may exist between the toxic power of the blood serum of the horse and of the guinea pig, and the power of these two serums to precipitate each other.

If we inject horse serum several times into a guinea pig we would expect to find that the blood serum of a guinea pig so treated would have a power of precipitating horse serum. This we found to be the case; but we could not find that the injection of a single small dose of horse serum into the guinea pig developed this power in the guinea pig's blood serum. We might, however, conjecture that the union of the two serums under the conditions named causes a precipitation which is not visible, or causes a chemical union between two highly organized albuminous substances having toxic properties. In order to test this subject more thoroughly we first made some experiments to determine the precipitating action of normal and antitoxic horse serum upon normal guinea-pig serum, as follows:

One c. c. of horse serum in dilution of 1:21 was placed in a small test tube. The 0.1 c. c. of normal guinea-pig serum was added to each tube. These were thoroughly shaken, placed in the incubator, and the results read after twenty-four hours.

Normal G. P. No. 1. Killed the same day with chloroform, blood defibrinated, and the serum separated in the centrifuge.

Normal G. P. No. 2. Killed by chloroform 3 days previously and the serum allowed to separate by coagulation.

(Two tests made of each serum.)

1 c. c. horse serum (1:21).	0.1 c. c. serum normal guinea pig 1.	0.1 c. c. serum normal guinea pig 2.
Normal horse serum (Sam).....	Nil.	Nil.
Normal horse serum (Jane).....	Nil.	Nil.
Antitoxic horse serum (Natl. VIII, 17).....	Nil.	Nil.
Antitoxic horse serum (Hubbert op. 1).....	Nil.	Nil.
Antitoxic horse serum (Natl. IX, 17).....	Slight precipi- tation(?).	Nil.
Antitoxic horse serum (Stearns 1110).....	Nil.	Nil.
	Nil.	Nil.
	Nil.	Nil.

From this and other similar experiments we are justified in concluding that neither normal horse serum nor antitoxic horse serum has any power to precipitate normal guinea-pig serum.

We next made some tests to determine whether a guinea pig previously treated with one small injection of horse serum developed precipitins.

One c. c. of horse serum both normal and antitoxic in dilution of 1:21 was placed in small tubes, as before, and 0.1 c. c. of a sensitized guinea-pig serum added to each tube, as shown in the table. They were shaken and placed in the incubator and results read after twenty-four hours.

G. P. No. 4617. [Previous treatment: 35 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (standard B27).]

G. P. No. 4510. [Previous treatment: same.]

1 c. c. horse serum (1:21).	0.1 c. c. normal guinea-pig serum.		0.1 c. c. treated guinea-pig serum.	
	Centrif- ugation.	Coagula- tion.	Guinea pig 4517.	Guinea pig 4510.
Normal horse serum (Sam).....	0	0	0	0
Normal horse serum (Jane).....	0	0	0	0
Normal horse serum (S. P.).....	0	0	0	0
Normal donkey serum.....	0	0	0	0
Antitoxic horse serum (Natl. VIII, 17).....	0	0	0	0
Antitoxic horse serum (Natl. V, 14).....	0	0	0	0
Antitoxic horse serum (Natl. IX, 17).....	+(?)	0	0	0
Antitoxic horse serum (Stearns 1110).....	0	0	0	0
Antitoxic horse serum (Stearns 1429).....	0	0	0	0

It would therefore appear that guinea pigs which have previously been inoculated with one injection of a very small amount of horse serum sufficient to render them highly susceptible to a second injection of horse serum do not contain sufficient precipitin in their

blood serum to cause a visible precipitation when added to horse serum.

The following studies show still more clearly that the specific precipitins have nothing to do with this toxic reaction.

We prepared guinea pigs by injecting them many times at short intervals with horse serum, so as to develop a high degree of precipitin in their blood serum against horse serum. The blood serum of guinea pigs so prepared was then added to horse serum in the proportions of about one of the former to two of the latter and allowed to stand until the precipitating action was complete. This guinea-pig serum was so active that very large quantities of the precipitum settled to the bottom of the test tubes. The mixture was now filtered, so as to separate the precipitum entirely, and the filtrate injected into sensitized guinea pigs and found to be quite as toxic as untreated horse serum.

G. P. No. 107. Seventeen subcutaneous injections of 1 c. c. each normal horse serum (roan) and one peritoneal injection of 6 c. c. antitoxic horse serum (Natl. IX, 19) were given between February 8 and March 11.

Six c. c. normal horse serum (roan) were mixed with 3 c. c. of the serum of this guinea pig and allowed to stand about 3 hours at room temperature. The large amount of precipitum which developed was filtered off and the filtrate injected into the following two guinea pigs:

G. P. No. 4996. Two c. c. of the above filtrate injected into peritoneal cavity. Dead in 20 minutes.

[Previous treatment: 27 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{700}$ c. c. antitoxic horse serum (Wellcome 474A).]

G. P. No. 5000. Five c. c. of the above filtrate injected into the peritoneal cavity. Dead in 10 minutes.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{700}$ c. c. antitoxic horse serum (Wellcome 477B).]

These experiments were repeated under varying conditions, especially allowing the two serums to remain in contact a longer time before filtering, and similar results obtained.

The results of this part of our work are strengthened by the conclusions of Pirquet and Schick, who found that the antibodies, whatever they may be, producing symptoms of the serum disease, are not identical with the precipitins. They found, for instance, that the symptoms of the serum disease appear within eight to thirteen days following the first injection of horse serum into man, whereas it requires about three weeks for precipitins to appear in the blood in children after the injection of horse serum.

The formation of precipitins does not take place as readily in man following the injection of horse serum as it does in rabbits. In fact, Pirquet and Schick found that sometimes even after the injection of 200 c. c. there was no production of precipitins, and, further, that the length of time that the precipitin reaction remains in the

blood of man following the injection is variable. It sometimes disappears in the fourth week, and sometimes is still markedly present in the ninth week.

Finally, we know that the precipitins are strictly specific, whereas the toxic action is only quantitatively specific.

EFFECT OF HEAT UPON THE TOXICITY OF HORSE SERUM.

One of the first questions which required solution was whether the toxic substance in blood serum is thermolabile. That it is able to withstand a comparatively high degree of heat for a long time, viz, 60° C. for six hours, is evident from the following experiments:

G. P. No. 4349. Six c. c. antitoxic horse serum (Natl. VIII. 17) heated to 60° C. for 30 minutes, then injected into the peritoneal cavity. Dead in 30 minutes.

G. P. No. 60. One c. c. same serum and injection as g. p. 4349. Dead in 10 minutes.

[Previous treatment: With toxine-antitoxin mixture.]

G. P. No. 61. Do. Dead in 10 minutes.

G. P. No. 62. Do. Symptoms; recovered.

G. P. No. 4897. Injected with 5 c. c. of an extract of normal horse serum (roan) heated to 60° C. for 6 hours. This degree of heat coagulated the serum. About 1 c. c. of the coagulum was added to 9 c. c. of salt solution, thoroughly shaken up, filtered, and the filtrate injected into the peritoneal cavity. Symptoms; death in about 3 hours.

[Previous treatment: 41 days prior, injected subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{300}$ c. c. horse serum (Alex. No. 192).]

G. P. No. 4508. Six c. c. of an extract of antitoxic horse serum (Natl. IX. 19) heated to 100° C. for 15 minutes, injected into the peritoneal cavity. The coagulum was ground up with a few c. c. of salt solution and strained through gauze before being injected. No symptoms.

One and a half hours later about 8 c. c. of the coagulum was ground up and the entire mass, not strained, injected into the peritoneal cavity of the same guinea pig. No symptoms.

G. P. No. 5048. Six c. c. of the coagulum of normal horse serum (roan) heated to 100° C. for 15 minutes and ground up with salt solution (0.85) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 20 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Alex. A204).]

From the above it is evident that while a temperature of 60° C. continued for six hours has practically no influence upon the toxic substance in horse serum, the toxicity is entirely destroyed by a temperature of 100° C. for fifteen minutes.

THE TOXIC PRINCIPLE IN HORSE SERUM IS FILTERABLE THROUGH PORCELAIN.

The following experiment is sufficient to demonstrate that the close-grained pores of a Pasteur-Chamberland filter B do not retain the toxic principle of horse serum:

G. P. No. 4521. Six c. c. of antitoxic horse serum (Natl. VIII. 17) filtered through a Pasteur-Chamberland filter B and injected into the peritoneal cavity. Dead in 35 minutes.

[Previous treatment: 32 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7 + 1 unit horse serum (Standard B27).]

DRYING DOES NOT INJURE THE TOXIC PRINCIPLE.

We have on hand a large quantity of dried antitoxic horse serum which has been prepared and preserved under special conditions for the preparation of the standard antitoxic unit. This serum was carefully dried under bacteriological precautions at a temperature below 37° C., as described in Bulletin No. 21.^a

That such dried and redissolved serum still retains its toxic property is evident from the following experiment:

G. P. No. 4376. Six c. c. antitoxic horse serum (B 1+12) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 19 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{250}$ c. c. horse serum (Natl. V. 7).]

THE TOXIC PRINCIPLE CAN NOT BE SEPARATED BY PRECIPITATION AND DIALYSIS.

We made several experiments to determine whether precipitation by ammonium sulphate and subsequent dialysis to remove the sulphate and other inorganic salts would also remove the toxic principle. For this purpose we used antitoxic horse serum prepared and dialysed in accordance with Gibson's method.^b It is plain from the following experiments that precipitation and dialysis do not remove the toxic principle:

G. P. No. 4104. Six c. c. antitoxic horse serum (NYBH A) injected into the peritoneal cavity. Dead in 5 minutes.

[Previous treatment: 37 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{250}$ c. c. horse serum (Alex. 190).]

G. P. No. 4506. Five c. c. antitoxic horse serum (Alex. A 203/NYBH) injected into the peritoneal cavity. No symptoms.^c

[Previous treatment: 25 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

G. P. No. 4513. Five c. c. antitoxic horse serum (Alex. A 203/NYBH) injected into the peritoneal cavity. Dead in 39 minutes.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

EFFECT OF VARIOUS CHEMICAL SUBSTANCES UPON THE TOXIC PRINCIPLE OF HORSE SERUM.

Various substances of widely different chemical nature were added to horse serum, in order to see whether any of them had the power of precipitating, oxidizing, or neutralizing the toxic property of the serum. The following substances were used: Succinic acid per-

^a Rosehau, M. J.: The immunity unit for standardizing diphtheria antitoxin (based on Ehrlich's normal serum); official standard prepared under the act approved July 1, 1902. Bulletin 21, Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service. Washington, Government Printing Office, April, 1905.

^b Gibson, R. B.: On the practical concentration of diphtheria antitoxin. *Am. med.*, vol. 10, 1905, p. 915.

^c Explanation of occasional irregularities, p. 63.

oxide (alphozone), butyric acid, hydrogen dioxide, permanganate of potash, alcohol, ammonium sulphate, and citrate of soda.

Butyric acid.

G. P. No. 4368. Ten c. c. of a $\frac{N}{10}$ butyric acid solution were added to 25 c. c. antitoxic horse serum (Natl. IX. 17); the mixture was kept at 15° C. for 40 hours, at the end of which time the fine precipitate which developed was filtered off and 3 c. c. injected into the peritoneal cavity. Dead in 2 hours 10 minutes.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{30}$ c. c. horse serum (Cutter 1461).]

Hydrogen dioxide.

G. P. No. 4371. Five c. c. of hydrogen dioxide (Oakland) were added to 25 c. c. antitoxic horse serum (Natl. IX. 19); the mixture was kept at 15° C. for 40 hours, at the end of which time a very little fine precipitate had formed, but the mixture effervesced in filtering; 3 c. c. of the filtrate was injected into the peritoneal cavity. Symptoms (?); recovery.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{270}$ c. c. horse serum (Cutter 1504).]

G. P. No. 4917. Five c. c. hydrogen dioxide (McKesson & Robbins) were added to 25 c. c. antitoxic horse serum (Natl. IX. 17); the mixture was kept at 15° C. for 40 hours, at the end of which time the fine precipitate which developed was filtered off, and 6 c. c. injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 41 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{180}$ c. c. antitoxic horse serum (Stearns 16H).]

Permanganate of potash.

G. P. No. 4370. Three c. c. of a 1 per cent solution of permanganate of potash were added to 25 c. c. antitoxic horse serum (Natl. IX. 19); the mixture was kept at 15° C. for 40 hours, and as no precipitate had formed in that time it was not filtered; 3 c. c. of the mixture inoculated into the peritoneal cavity. Dead in 45 minutes.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{430}$ c. c. horse serum (Cutter 1461).]

Succinic peroxide acid (alphozone).

G. P. No. 4372. Five c. c. of a 1 per cent solution of alphozone were added to 25 c. c. antitoxic horse serum (Natl. IX. 19); the mixture was kept at 15° C. for 40 hours; the precipitate which formed was filtered off and 3 c. c. of the filtrate injected into the peritoneal cavity. No symptoms.^a

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Cutter 1504).]

G. P. No. 5A. Ten c. c. of the same filtrate injected into the peritoneal cavity. Dead in 35 minutes.

[Previous treatment: 30 days prior, inoculated with 0.22 c. c. toxine No. 7 + 1 unit of horse serum (Standard B27).]

As we found that 2 c. c. of a 1 per cent solution of succinic peroxide acid (alphozone) injected into the peritoneal cavity of a normal guinea pig produced transient irritating effects these experiments were repeated, using smaller quantities of the acid, as follows:

^a Explanation of occasional irregularities, p. 63.

G. P. No. 4519. One c. c. of a 1 per cent solution of alphozone was added to 25 c. c. antitoxic horse serum (Natl. IX. 19); the mixture was kept at 15° C. for 40° hours; the precipitate which formed was filtered off and 6 c. c. of the filtrate injected into the peritoneal cavity. Dead in 24 minutes.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

G. P. No. 4518. Five c. c. added as above and 6 c. c. of the filtrate injected into the peritoneal cavity. Dead in 25 minutes.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

Alcohol.

G. P. No. 4373. Five c. c. of 95 per cent alcohol were added to 25 c. c. antitoxic horse serum (Natl. IX. 19); the mixture was kept at 15° C. for 40 hours; the precipitate which formed was filtered off and 3 c. c. of the filtrate injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{3\frac{1}{10}}$ c. c. horse serum (Cutter 1504).]

G. P. No. 5B. Seven and a half c. c. added as above and 3 c. c. of the filtrate injected into the peritoneal cavity. No symptoms.^a

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

G. P. No. 156. Seven and a half c. c. added as above and 6 c. c. of the filtrate injected into the peritoneal cavity. Dead in 90 minutes.

[Previous treatment: 60 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{3\frac{1}{10}}$ c. c. antitoxic horse serum (Stearns 1351).]

G. P. No. 4363. Ten c. c. added as above and 3 c. c. of the filtrate injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{2\frac{1}{10}}$ c. c. horse serum (P D & Co .07173-G).]

G. P. No. 4C. Twenty-five c. c. added as above. This caused practically solid coagulation on the serum. The coagulent was vigorously shaken up with salt solution (0.85) and filtered by the aid of a vacuum, and 6 c. c. of the opalescent filtrate injected into the peritoneal cavity. Dead in 4 hours 10 minutes.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

Ammonium sulphate.

We know from the work done with serum precipitated with ammonium sulphate and subsequently dialysed that the ammonium sulphate has no action upon the toxic principle found in horse serum. (See guinea pigs Nos. 4104, 4106, and 4513, p. 39.)

Citrate of soda.

We know that citrate of soda has no injurious action upon the toxic principle found in horse serum because some of the serum we used was prepared by adding 1 per cent solution of citrate of soda to the whole blood as it was drawn from the horse in order to prevent

^a For explanation of occasional irregularities, see p. 63.

clotting and the clear serum subsequently pipetted off. The citrate of soda was afterwards removed by dialysis (Gibson's method) and the plasma proved just as toxic to treated guinea pigs as other horse serum. We also have the following experimental data upon this point:

G. P. No. 4925. Six c. c. normal horse serum (roan) containing 1 per cent citrate soda injected into the peritoneal cavity. Dead in 15 minutes.

[Previous treatment: 39 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{300}$ c. c. antitoxic horse serum (Cutter 1465).]

G. P. No. 4918. Injected as above. Dead in 5 minutes.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{230}$ c. c. antitoxic horse serum (Stearns 16 H).]

G. P. (control). The above guinea pigs were controlled by injecting 6 c. c. of the same serum containing 1 per cent citrate of soda into the peritoneal cavity of a normal pig. The only effects of this inoculation were symptoms of irritation which soon passed away.

INFLUENCE OF ANTISEPTICS, ETC.

As much of this work was done with horse serum preserved by means of chloroform and trikresol (0.4 per cent) we made a control experiment, using horse serum as fresh as possible without the addition of any substance. The following experiment eliminates these factors as having any influence upon the toxicity of the serum:

G. P. No. 125. Three c. c. normal horse serum (roan) freshly drawn, centrifugized and injected into the peritoneal cavity as soon as the serum separated. Dead in 45 minutes.

[Previous treatment: 49 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns 1351).]

EFFECT OF OLD HORSE SERUM UPON SUSCEPTIBLE GUINEA PIGS.

At one time in our work it appeared to us that the toxic properties of horse serum gradually diminished in toxicity with the age of the serum. It was, however, soon proved by the following experiments that very old serums may be quite as poisonous as those freshly drawn.

G. P. No. 4496. Four c. c. antitoxic horse serum (Natl. V. 2) injected into the peritoneal cavity. The serum was at least *one and a half years old* when injected. Dead in 30 minutes.

[Previous treatment: 25 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit of horse serum (Standard B27).]

G. P. No. 4921. Six c. c. antitoxic horse serum *over 3 years old* (P. D. & Co .0495 prepared Dec. 15, 1902) inoculated into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 39 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{300}$ c. c. antitoxic horse serum (Cutter 1465).]

G. P. No. 4922. Same injection. No symptoms.^a

[Previous treatment: 39 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{400}$ c. c. antitoxic horse serum (Cutter 1465).]

G. P. No. 4899. Same injection. Dead in 6 minutes.

[Previous treatment: 48 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{350}$ c. c. antitoxic horse serum (Alex. 192).]

^a Explanation of occasional irregularities, p. 63.

The following guinea pigs were inoculated with horse serum eight and one-half years old:

G. P. No. 258. Six c. c. antiamarillic serum injected into the peritoneal cavity. Dead in 40 min.

[Previous treatment: 24 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. normal horse serum (roan) heated to 60° C. for two hours.]

G. P. No. 256. Same injection. Symptoms, recovered.

[Previous treatment: 20 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. normal horse serum (roan) heated to 60° C. for two hours.]

From the above experiments we see that blood serum over eight and one-half years old is as poisonous to sensitized pigs as fresh serum.

EFFECT OF X-RAYS UPON THE TOXIC PRINCIPLE.

Normal horse serum (roan) was exposed to the action of X rays, 40 amperes, 4 inches from the tube for forty minutes, then injected into a susceptible guinea pig. It was found as poisonous as horse serum not so treated.

G. P. No. 6A. Six c.c. above serum injected into peritoneal cavity. Dead in 10 minutes.

[Previous treatment: 33 days prior, inoculated subcutaneously with 0.293 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B28).]

Part V.

THE INFLUENCE OF TIME.

TIME NECESSARY TO RENDER A GUINEA PIG SUSCEPTIBLE.

We know from our preliminary work that some time is necessary after the first injection of horse serum before a guinea pig is rendered susceptible to the toxic action of a second injection. The following series demonstrates that this time is about ten days:

G. P. No. 4464. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: *5 days* prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

G. P. No. 4485. Six c. c. same serum and injection as g. p. 4484. No symptoms.

[Previous treatment: *6 days* prior, as g. p. 4484.]

G. P. No. 4486. Six c. c. same serum and injection as g. p. 4484. No symptoms.

[Previous treatment: *7 days* prior, as g. p. 4484.]

G. P. No. 4533. Six c. c. same serum and injection as g. p. 4484. No symptoms.

[Previous treatment: *8 days* prior, as g. p. 4484.]

G. P. No. 4530. Six c. c. same serum and injection as g. p. 4484. Symptoms; recovered.

[Previous treatment: *10 days* prior, as g. p. 4484.]

G. P. No. 4532. Six c. c. same serum and injection as g. p. 4484. Symptoms; recovered.

[Previous treatment: *11 days* prior, as g. p. 4484.]

G. P. No. 4488. Six c. c. same serum and injection as g. p. 4484. Dead in 10 minutes.

[Previous treatment: *12 days* prior, as g. p. 4484.]

G. P. No. 4525. Six c. c. same serum and injection as g. p. 4484. Dead in 45 minutes.

[Previous treatment: *12 days* prior, as g. p. 4484.]

G. P. No. 4487. Six c. c. same serum and injection as g. p. 4484. Dead in 60 minutes.

[Previous treatment: *13 days* prior, as g. p. 4484.]

G. P. No. 4531. Six c. c. same serum and injection as g. p. 4484. Dead in 45 minutes.

[Previous treatment: *13 days* prior, as g. p. 4484.]

G. P. No. 4476. Six c. c. same serum and injection as g. p. 4484. Dead in 10 minutes.

[Previous treatment: *14 days* prior, inoculated subcutaneously with 0.22 c. c. toxine No 7+ $\frac{1}{200}$ c. c. antitoxic serum (Natl. IX. 18).]

G. P. No. 4490. Six c. c. same serum and injection as g. p. 4484. Dead in 46 minutes.

[Previous treatment: *14 days* prior, as g. p. 4484.]

G. P. No. 4529. Six c. c. same serum and injection as g. p. 4484. Dead in 47 minutes.

[Previous treatment: *15 days* prior, as g. p. 4484.]

THE GUINEA PIG REMAINS SUSCEPTIBLE A VERY LONG TIME.

That the guinea pig remains susceptible to the toxic action of horse serum a very long time is indicated in the following experiments in which 160 days elapsed between the first treatment and the second

injection. How much longer this action may continue will be ascertained and reported upon at a subsequent time.

G. P. No. 4507. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Dead in 20 minutes.

[Previous treatment: 60 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+1 unit horse serum (Standard B27).]

G. P. No. 4A. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Dead in 22 minutes.

[Previous treatment: 84 days prior, inoculated subcutaneously with 0.293 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

G. P. No. 3827. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Dead in 33 minutes.

[Previous treatment: 160 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{330}$ c. c. horse serum (Jordan No. 201).]

Part VI.

DOSAGE AS A FACTOR.

MINIMAL AMOUNT OF HORSE SERUM NECESSARY TO RENDER A GUINEA PIG SUSCEPTIBLE.

A large part of our work was done upon guinea pigs which had been used to measure the strength of antitoxic serums. As the strength of diphtheria antitoxin runs between 250 and 1,000 units to the c. c. most of our guinea pigs were therefore rendered susceptible by doses of horse serum varying from $\frac{1}{250}$ to $\frac{1}{1000}$ c. c. It now becomes interesting to know how small a quantity of horse serum injected into a healthy guinea pig would render it susceptible to the toxic action of horse serum.

G. P. No. 217. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 45 days prior, inoculated subcutaneously with $\frac{1}{100}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 219. Do.

G. P. No. 216. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 24 days prior, inoculated subcutaneously with $\frac{1}{100}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 222. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 24 days prior, inoculated subcutaneously with $\frac{1}{1000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 223. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 130 minutes.

[Previous treatment: 45 days prior, inoculated subcutaneously with $\frac{1}{1000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 220. Do. Dead in 68 minutes.

G. P. No. 225. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 24 days prior, inoculated subcutaneously with $\frac{1}{10000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 224. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 45 days prior, inoculated subcutaneously with $\frac{1}{10000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 227. Do.

G. P. No. 229. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms; recovered.

Previous treatment: 24 days prior, inoculated subcutaneously with $\frac{1}{1000000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 230. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 45 days prior, inoculated subcutaneously with $\frac{1}{1000000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 228. Do.

G. P. No. 232. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 24 days prior, inoculated subcutaneously with $\frac{1}{1000000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 235. Do.

G. P. No. 234. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into peritoneal cavity. No symptoms.

[Previous treatment: 30 days prior, inoculated subcutaneously with $\frac{1}{1000000}$ c. c. antitoxic horse serum (Natl. IX. 19).]

G. P. No. 233. Do. Symptoms; recovered.

It is plain from the above series that guinea pigs may be sensitized with very small amounts of horse serum. Guinea pig No. 233 received only $\frac{1}{1000000}$ of a c. c. at the first injection and this quantity was sufficient to render it susceptible to a subsequent injection of horse serum.

MINIMAL AMOUNT OF HORSE SERUM NECESSARY TO POISON A SUSCEPTIBLE GUINEA PIG.

From the following series of guinea pigs it will be seen that the toxic principle must be present in exceedingly small quantities of horse serum.

G. P. No. 4348. Four c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 30 minutes.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. $5 + \frac{1}{440}$ antitoxic horse serum (PD 08021).]

G. P. No. 4099. Three c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 15 minutes.

[Previous treatment: 37 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + \frac{1}{110}$ c. c. antitoxic horse serum (Alex. 190).]

G. P. No. 3954. Three c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 57 minutes.

[Previous treatment: 51 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. $5 + \frac{1}{310}$ c. c. antitoxic horse serum (Hubbert 1).]

G. P. No. 4364. Three c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. Dead in 45 minutes.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. $7 + \frac{1}{300}$ c. c. antitoxic horse serum (PD 07173).]

G. P. No. 4350. Two c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 15 minutes.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. $5 + \frac{1}{430}$ c. c. antitoxic horse serum (PD 08021).]

G. P. No. 4352. One c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 35 minutes.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{460}$ c. c. antitoxic horse serum (PD 08021).]

G. P. No. 4101. One c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 37 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic horse serum (Alex. 190).]

G. P. No. 4511. One c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 35 minutes.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7 + 1 unit antitoxic horse serum (Standard B27).]

G. P. No. 4512. One c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Dead in 81 minutes.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7 + 1 unit antitoxic horse serum (Standard B27).]

G. P. No. 4623. One c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{300}$ c. c. antitoxic horse serum (Alex. 192).]

G. P. No. 4514. Two-tenths c. c. antitoxic horse serum (Natl. VIII. 17) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7 + 1 unit antitoxic horse serum (Standard B27).]

G. P. No. 4520. Two-tenths c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 65 minutes.

[Previous treatment: 42 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7 + 1 unit antitoxic horse serum (Standard B27).]

G. P. No. 130. One-tenth c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Dead in 55 minutes.

[Previous treatment: 45 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns 1351).]

G. P. No. 151. One-tenth c. c. antitoxic horse serum (Natl. IX. 19) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 45 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns).]

G. P. No. 136. Do. Symptoms; recovered.

G. P. No. 144. Do. No symptoms.

G. P. No. 165. One hundredth c. c. antitoxic horse serum (Natl. IX. 17) inoculated subcutaneously. No symptoms.

3 hrs. 45 min. later, 0.1 c. c. Do. Symptoms; recovered.

[Previous treatment: 45 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Stearns 1351).]

G. P. No. 148. One-hundredth c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.

3 hrs. 45 min. later, 0.1 c. c. subcutaneously. Symptoms; recovered.

It will be seen from the above series that one-tenth of a cubic centimeter of horse serum into the peritoneal cavity of a susceptible guinea pig is sufficient to cause the death of the animal, whereas the same quantity subcutaneously causes symptoms.

THE INFLUENCE OF LARGE QUANTITIES IN RENDERING GUINEA PIGS
SUSCEPTIBLE.

The guinea pigs in the following series were first used as controls to show that the injection of large quantities of horse serum into the peritoneal cavity produces no effect. They were subsequently injected with horse serum again in large quantities into the peritoneal cavity to determine their susceptibility:

G. P. No. 296. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 14 days prior, 6 c. c. donkey serum injected into the peritoneal cavity.]

G. P. No. 297. Do.

G. P. No. 298. Same injection. No symptoms.

[Previous treatment: 14 days prior, 6 c. c. normal horse serum (Sp.) injected into the peritoneal cavity.]

G. P. No. 299. Do. Symptoms; recovered.

G. P. No. 300. Same injection. Symptoms; recovered.

[Previous treatment: 22 days prior, 6 c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity.]

G. P. No. 301. Do.

G. P. No. 302. Same injection. Symptoms; recovered.

[Previous treatment: 14 days prior 6 c. c. antitoxic horse serum (Natl. V. 14) injected into the peritoneal cavity.]

G. P. No. 303. Do. Symptoms (?)

G. P. No. 304. Same injection. Dead in 65 minutes.

[Previous treatment: 14 days prior 6 c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity.]

G. P. No. 305. Do. Dead in 95 minutes.

G. P. No. 306. Same injection. Symptoms; recovered.

[Previous treatment: 14 days prior, 3.5 c. c. antitoxic horse serum (NYBH 10B Gibson) injected into the peritoneal cavity.]

G. P. No. 307. Same injection. Dead in 48 minutes.

[Previous treatment: 14 days prior, 2 c. c. antitoxic horse serum (NYBH 13C Gibson) injected into the peritoneal cavity.]

G. P. No. 308. Same injection. Dead in 43 minutes.

[Previous treatment: 14 days prior, 3 c. c. antitoxic horse serum (Alex. A211) injected into the peritoneal cavity.]

G. P. No. 309. Same injection. Symptoms; recovered.

[Previous treatment: 14 days prior, 6 c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity.]

G. P. No. 310. Do. Symptoms; recovered.

It is plain, therefore, that guinea pigs may be rendered susceptible by the injection of large amounts of horse serum into the peritoneal cavity. We have seen, in another part of this bulletin, that these animals may also be rendered susceptible by the injection of large amounts into the subcutaneous tissue.

We believe, however, that guinea pigs are rendered more susceptible by the injection of the toxine-antitoxin mixture than by the horse serum alone.

Part VII.

SENSITIZING SUBSTANCE.

We already know that guinea pigs may be sensitized with either normal or antitoxic horse serum. It is of course both interesting and important to know whether the substance contained in horse serum which renders the guinea pigs sensitive is the same as the substance which exerts its poisonous action upon the second injection.

GUINEA PIGS MAY BE SENSITIZED WITH PRECIPITATED AND DIALYZED SERUM.

The following examples selected from our work demonstrate this point:

G. P. No. 4972. One c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 22 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{800}$ c. c. antitoxic horse serum (NYBH 13C, precipitated and dialyzed in accordance with Gibson's method).]

G. P. No. 4973. Do.

G. P. No. 4955. Six c. c. same serum. Dead in 27 minutes.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{400}$ c. c. antitoxic horse serum (NYBH 10B).]

G. P. No. 4957. Same injection. Symptoms; recovered.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5+ $\frac{1}{300}$ c. c. antitoxic horse serum (NYBH 10B).]

DRYING DOES NOT INJURE THE SENSITIZING SUBSTANCE.

A number of guinea pigs which were used by us in this work were sensitized with the antitoxic serum preserved under special conditions in this laboratory as the official standard in accordance with the law of July 1, 1902. This serum was reduced to dryness under special conditions and must be redissolved before using. Compare page 39.

The following are selected as experimental data proving that drying does not injure the sensitizing substance:

G. P. No. 6B. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Dead in 27 minutes.

[Previous treatment: 86 days prior inoculated subcutaneously with 0.22 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B25).]

G. P. No. 4488. Same injection. Dead in 10 minutes.

[Previous treatment: 12 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

SMALL QUANTITIES OF HORSE SERUM MAY RENDER GUINEA PIGS MORE SUSCEPTIBLE THAN LARGE QUANTITIES.

Before we learned that the antitoxin contained in the blood serum of the horse plays no rôle in rendering guinea pigs susceptible to subsequent inoculations of horse serum we planned and carried out an extensive series of experiments to determine just what relation the susceptibility of guinea pigs bears to the antitoxic potency of the horse serum injected. One series of guinea pigs was injected subcutaneously with one unit of an antitoxic horse serum containing 250 units to the c. c. This series, therefore, received $\frac{1}{250}$ c. c. of horse serum. The second series was treated subcutaneously with 250 units—that is, the guinea pigs received 1 c. c. of the horse serum. The third series of guinea pigs was treated with 1,000 units—that is, each guinea pig received 4 c. c. of the antitoxic horse serum. At varying intervals following these injections the pigs were given a second injection of horse serum in order to determine their susceptibility.

The following guinea pigs received $\frac{1}{250}$ c. c. antitoxic horse serum containing 1 unit:

G. P. No. 18. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity.

[Previous treatment: 1 day prior, inoculated subcutaneously with 1 unit, viz, $\frac{1}{250}$ c. c., horse serum (Natl. IX. 18).] No symptoms.

G. P. No. 17. Same injection as g. p. 18. No symptoms.

[Previous treatment: 4 days prior, as g. p. 18.]

G. P. No. 11. Same injection as g. p. 18. Dead in 35 minutes.

[Previous treatment: 17 days prior, as g. p. 18.]

G. P. No. 16. Same injection as g. p. 18. Symptoms; recovered.

[Previous treatment: 18 days prior, as g. p. 18.]

G. P. No. 15. Same injection as g. p. 18. Dead in 18 minutes.

[Previous treatment: 24 days prior, as g. p. 18.]

G. P. No. 19. Same injection as g. p. 18. Symptoms; recovered.

[Previous treatment: 32 days prior, as g. p. 18.]

G. P. No. 12. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into peritoneal cavity. Dead in 44 minutes.

[Previous treatment: 47 days prior, as g. p. 18.]

G. P. No. 10. Six c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 47 days prior, as g. p. 18.]

G. P. No. 13. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 68 days prior, as g. p. 18.]

The following guinea pigs received 1 c. c. antitoxic horse serum containing 250 units:

G. P. No. 29. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 1 day prior, inoculated subcutaneously with 250 units, viz, 1 c. c., horse serum (Natl. IX. 18).]

- G. P. No. 27. Same injection as g. p. 29. No symptoms.
[Previous treatment: 4 days prior, as g. p. 29.]
- G. P. No. 28. Same injection as g. p. 29. Symptoms; recovered.
[Previous treatment: 17 days prior, as g. p. 29.]
- G. P. No. 26. Same injection as g. p. 29. Symptoms; recovered.
[Previous treatment: 18 days prior, as g. p. 29.]
- G. P. No. 25. Same injection as g. p. 29. Symptoms; recovered.
[Previous treatment: 24 days prior, as g. p. 29.]
- G. P. No. 23. Same injection as g. p. 29. Symptoms; recovered.
[Previous treatment: 32 days prior, as g. p. 29.]
- G. P. No. 24. Six c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. Dead in 45 minutes.
[Previous treatment: 47 days prior, as g. p. 29.]
- G. P. No. 22. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 47 days prior, as g. p. 29.]
- G. P. No. 21. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Dead in 44 minutes.
[Previous treatment: 67 days prior, as g. p. 29.]
- G. P. No. 20. Four c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 83 days prior, as g. p. 29.]

The following guinea pigs received 4 c. c. of antitoxic horse serum containing 1,000 units:

- G. P. No. 38. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.
[Previous treatment: 1 day prior, inoculated subcutaneously with 1,000 units, viz, 4 c. c., antitoxic horse serum (Natl. IX. 18).]
- G. P. No. 35. Same injection as g. p. 38. No symptoms.
[Previous treatment: 4 days prior, as g. p. 38.]
- G. P. No. 36. Same injection as g. p. 38. Symptoms; recovered.
[Previous treatment: 17 days prior, as g. p. 38.]
- G. P. No. 32. Same injection as g. p. 38. Symptoms; recovered.
[Previous treatment: 18 days prior, as g. p. 38.]
- G. P. No. 34. Same injection as g. p. 38. Symptoms; recovered.
[Previous treatment: 24 days prior, as g. p. 38.]
- G. P. No. 37. Same injection as g. p. 38. No symptoms.
[Previous treatment: 32 days prior, as g. p. 38.]
- G. P. No. 39. Six c. c. antitoxic horse serum (Natl. IX. 17) injected into the peritoneal cavity. No symptoms.
[Previous treatment: 47 days prior, as g. p. 38.]
- G. P. No. 31. Six c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 47 days prior, as g. p. 38.]
- G. P. No. 33. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Dead in 46 minutes.
[Previous treatment: 68 days prior, as g. p. 38.]
- G. P. No. 30. Four c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.
[Previous treatment: 83 days prior, as g. p. 38.]

We see from the above series that it required 17 days (or less) for the guinea pigs to become susceptible.

We learn from these three series that guinea pigs receiving 4 c. c. of antitoxic horse serum are apparently not quite so susceptible as those receiving the smaller amounts ($\frac{1}{250}$ c. c. and 1 c. c.); also, that those which received 1 c. c. are apparently not quite so susceptible as those which received only $\frac{1}{250}$ c. c. of the horse serum. From our work we know that it is the quantity of horse serum, and not the number of units contained in the serum, which plays the important rôle. If this relation of the amount of serum is true, we presume that animals receiving large quantities of horse serum for the first injection are less susceptible because they are rendered slightly immune, just as animals may be immunized against this action by daily repeated inoculations. When large quantities are given at the first injection, the horse serum is probably absorbed very slowly and acts somewhat in the same manner.

It would also seem from the above that guinea pigs are not rendered quite as susceptible by first injections of horse serum as by injections of the toxine-antitoxin mixture.

THE SENSITIZING SUBSTANCE IS NOT FREE IN THE BLOOD SERUM.

The following work seems to indicate that the substance which renders the guinea pigs susceptible to a second injection of horse serum is not free in the blood serum of the guinea pig in the same sense that the free receptors are in diphtheria antitoxic serum:

G. P. No. 298 (normal). Eight c. c. of a mixture containing 4 c. c. serum of susceptible guinea pigs and 4 c. c. normal horse serum, injected into the peritoneal cavity; the serums were mixed and injected at once. No symptoms.

G. P. No. 299. Ten c. c. above mixture injected into the peritoneal cavity. No symptoms.

G. P. No. 297. Five c. c. above mixture injected into the peritoneal cavity. No symptoms.

From the fact that the sensitizing substance does not appear to be free in the blood of the guinea pig and from the further fact that we were unable to transfer the immunity we might infer that this reaction may not reside so much in the blood serum as in the cells of the body.

THE EFFECT OF HEAT UPON THE SENSITIZING SUBSTANCE.

The following experiments plainly prove that the sensitizing substance is very resistant to heat, for guinea pigs previously treated with small quantities of horse serum heated to 60° C. for six hours subsequently proved highly susceptible:

G. P. No. 265. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 38 minutes.

[Previous treatment: 17 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. normal horse serum (roan) heated to 60° C. for 6 hours.]

G. P. No. 266. Do. Dead in 20 minutes.

G. P. No. 267. Do. Dead in 25 minutes.

Part VIII.

ACTION OF HORSE SERUM UPON MAN AND OTHER ANIMALS.

MAN.

It may be that man can not be sensitized in the same way that we have shown is the case with guinea pigs. We made no human experiments, but have experimental data done by others which has a direct bearing on this question.

Pirquet and Schick injected children with antitoxic horse serum at intervals.

It has been customary to immunize numbers of children when exposed to diphtheria with antitoxic horse serum at intervals of from three to four weeks.

We have no doubt that there are many such instances on record and, so far as we know, this practice has never caused death.

Repeated injections of horse serum into man is not an infrequent occurrence. Patients suffering with diphtheria are often given injections of antitoxic serum at short and frequent intervals. It is also not rare for persons to have several attacks of diphtheria at long intervals and to be treated each time with antidiphtheric serum.

Certain serums, for example, the antitubercle serum of Maragliano, or the antirheumatic serum of Menzer are habitually used by giving injections at intervals of days or weeks.

In all of these cases of frequent and repeated injections the amount which has been injected and the interval between the injections must be taken into account in relation to this work. Pirquet and Schick in their work on Serumkrankheit give the following instances in which children received two injections of horse serum at intervals of from sixteen to forty-two days between the first and second injections.

Leopold H.—October 3, 1902. 100 c. c. scarlet-fever serum (Moser). Eight days following this injection symptoms of the serum disease appeared and lasted several weeks.

December 2, 1902. Fifty days after the first injection patient received 2 c. c. antidiphtheric serum under skin of arm.

In fifteen minutes following this second injection stormy symptoms set in. The boy began to cry and complained of nausea. Edema of the lip set in and soon spread over the whole face. In several hours general urticaria.

Heinrich K.—Three years old. June 13, 1902. 100 c. c. scarlet-fever serum. On the eighth day following the injection, symptoms of the serum disease appeared which lasted until the twenty-sixth day.

July 7. Thirty-four days following the first injection, 1 c. c. antidiphtheric serum injected into the left arm. The same afternoon urticaria and swelling of the lips. The next morning the arm was highly edematous.

Alexandrine K. Nine years old. May 28, 1902. 180 c. c. normal horse serum. Eleven days after the injection severe symptoms appeared, which lasted until June 17.

Sixteen days following the first injection, given 1 c. c. diphtheric antitoxic serum in the right forearm. Next morning, the hand swollen, very painful, and smartly to such an extent that the infection was considered of an erysipelatous nature. All redness and swelling disappeared in a few days.

Elizabeth K. Six and one-half years old. May 3, 1902. Given 180 c. c. scarlet-fever serum. May 15, ten days following, sudden rise of temperature, 39.4° C. Swelling of the lymph nodes. No exanthem.

Nineteen days after the first injection 50 c. c. scarlet-fever serum, following which occurred severe and painful edema of the skin of the abdomen, which spread to the labia and thighs, and disappeared in about a week.

Franz Z. June 6, 1903. 1 c. c. antidiphtheric serum. June 16 had urticaria, about nine days after the injection. August 2, eight weeks after first injection again given 5 c. c. antidiphtheric serum. Shortly following, urticaria and swelling of the face.

Frieda Z. June 10, 1903. 1 c. c. antidiphtheric serum. June 26, sixteen days following, the same injection repeated and acted in all respects similar to the above case, Franz Z., her brother. On August 2 she was again given 5 c. c. antidiphtheric serum. One hour later her face became red and swollen. The lids became so edematous that she could not open her right eye. In two hours there was general urticaria. Temperature, 38.6° C. Moderate swelling, locally.

Elli M. Four months old. First injection June 20, 1904. 12 c. c. antidiphtheric serum. Ten days later sudden rise of temperature 39° C. and urticaria. The fever lasted two days. Eruption later became measles-like and remained several days.

Nineteen days after the first injection 5 c. c. antidiphtheric serum. One hour after this severe general urticaria. From the site of injection, swelling of the skin of the abdomen. In the afternoon the temperature rose to 39.5° C.; frequent vomiting.

Leopoldine K. December 1, 1903. 5 c. c. horse serum. Twenty-seven days following the first injection, patient received 1 c. c. antidiphtheric serum. One hour following this last injection, definite swelling of the right hand, which later spread to the entire arm.

All these eight cases show this in common, that after the first injection of horse serum, the symptoms of the serum disease appear after the normal period of incubation, namely, between the eighth to thirteenth day. But when the same individuals are again injected with horse serum after intervals of sixteen to forty-two days, there reappears at once, or at least within twenty-four hours, symptoms of the serum disease.

Von Pirquet and Schick further give a list of 60 children who were injected with antitoxic horse serum at intervals from six days to seven and a half years between the first and second injections. They found that when the second injection was given from fourteen days to four months after the first injection they obtained, with great regularity, what they termed "the immediate reaction," but

when the interval between the first and second injection is over four months they obtained little or no immediate reaction, but what they termed "an accelerated reaction," for the fever, urticaria, and other symptoms of the serum disease appeared on the fifth, sixth, seventh, or eighth day. It will be remembered that the normal period of incubation for the symptoms of the serum disease to appear after the first injection is between the eighth and thirteenth day. Von Pirquet and Schick lay special stress upon the phenomena of the "immediate" and "accelerated" reactions following the second injection.

We might also conclude despite the suggestion contained in Part X of our work upon sensitizing guinea pigs by feeding them with horse serum or horse meat that children may not be sensitized to the toxic action in horse serum by eating horse meat from the fact that horse meat is a favorite article of diet in certain European countries, and there is nothing on record to show that the injection of horse serum in those countries is fraught with more danger than where this practice does not obtain. We must, however, remember that our work has shown that guinea pigs are sensitized with exceedingly minute quantities of the strange proteid, and that repeated injections cause an immunity; and it is possible that the same action may be true of feeding.

Man reacts to the first injection of horse serum after a period of incubation of eight to thirteen days. Guinea pigs show practically no reaction following the first injection. Both react to a second injection. The reactions in man and the guinea pig, however, differ both in severity and kind. The relation, therefore, that our observations upon the guinea pig may have in its application to man must await further study. Of course, the fact that other animals besides man and guinea pigs react to a second injection of horse serum would seem to indicate that we are dealing with one and the same action.

We have tested monkeys, rabbits, mice, dogs, cats, rats, chickens, and pigeons to determine whether any of these animals may be sensitized to the action of horse serum. Thus far we have obtained a response in the dogs, rabbits, and cats. This work is still in progress and will be reported at a future date.

Von Pirquet and Schick also found that the first injection into rabbits caused no clinical effect, but that subsequent subcutaneous injections caused immediate reaction in the production of local edema which extended even to gangrene. Second injections, when introduced intravenously, produced symptoms of collapse and even death.

Arthus also found that the injection of horse serum into rabbits caused no symptoms, whether the horse serum was injected subcutaneously or intravenously, but when he injected the serum every six days subcutaneously he obtained, after the fourth injection, edema and local reaction which continued to gangrene.

A rabbit which von Pirquet and Schick had previously treated with 8 injections was then given 2 c. c. of horse serum into the ear vein. The rabbit reacted to this in a minute and, after characteristic symptoms similar to those we see in guinea pigs, died in about four minutes.

Arthus obtained similar results with repeated injections of sterilized milk.

Part IX.

IMMUNITY.

ACTIVE IMMUNITY.

GUINEA PIGS MAY BE IMMUNIZED AGAINST THE TOXIC SUBSTANCE IN HORSE SERUM.

Guinea pigs may be immunized against this toxic substance, following the lines of active immunity produced by repeated inoculations of bacterial toxins. For instance, a guinea pig that has received an injection daily for ten days of small quantities (1 c. c.) of horse serum develops a high degree of immunity to subsequent injections of horse serum. Guinea pigs that have received more than ten inoculations on ten successive days develop a still higher degree of immunity.

G. P. No. 109. Six c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 15 to 27 days prior, 10 subcutaneous inoculations, 1 c. c. each, of antitoxic horse serum (Natl. IX. 19).]

G. P. No. 111. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 36 to 48 days prior, 10 subcutaneous inoculations, 1 c. c. each, normal horse serum (Sam).]

G. P. No. 107. Six c. c. antitoxic horse serum (Natl. IX. 19) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 15 to 27 days prior, 10 subcutaneous inoculations, 1 c. c. each, normal horse serum (Sam).]

G. P. No. 106. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 36 to 48 days prior, 10 subcutaneous inoculations, 1 c. c. each, normal horse serum (Sam).]

G. P. No. 108. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Symptoms; recovered.

[Prior treatment: 37 to 50 days prior, 10 subcutaneous inoculations, 1 c. c. each, normal horse serum (Sam).]

6 days later, 1 c. c. normal horse serum (roan) inoculated subcutaneously on each of 12 successive days. No symptoms.

6 days later, 6 c. c. normal horse serum (roan) into peritoneal cavity. No symptoms.

G. P. No. 110. Six c. c. antitoxic horse serum (Natl. VIII. 18) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 37 to 50 days prior, 10 subcutaneous inoculations, 1 c. c. each, antitoxic horse serum (Natl. IX. 19).]

6 days later, 1 c. c. normal horse serum (roan) inoculated subcutaneously on each of 12 successive days. No symptoms.

6 days later, 6 c. c. normal horse serum (roan) into peritoneal cavity. No symptoms.

We noticed that the subcutaneous injection of horse serum into guinea pigs sometimes occasions a local reaction, as indicated by edema at the site of inoculation, but the above guinea pigs Nos. 108 and 110, which received a large number of injections, seemed to react less each time.

We give below a series of 11 guinea pigs injected with large quantities of horse serum at irregular intervals. It is plain from these experiments that a rather high degree of immunity may be induced by repeated injections.

G. P. No. 4101. One c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 37 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{100}$ c. c. antitoxic horse serum (Alex. 190).]

8 days later, 1 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. Symptoms, less severe.

16 days later, 6 c. c. into peritoneal cavity. No symptoms.

6 days later, 6 c. c. into peritoneal cavity. Symptoms.

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

34 days later, 6 c. c. into peritoneal cavity. Symptoms (?).

20 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. No symptoms.

G. P. No. 4530. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 10 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7+1 unit antitoxic horse serum (Standard B27).]

15 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. Symptoms.

2 days later, 6 c. c. into peritoneal cavity. Restless.

6 days later, 6 c. c. into peritoneal cavity. Symptoms (?).

9 days later, 6 c. c. into peritoneal cavity. Symptoms (?).

33 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. No symptoms.

21 days later, 6 c. c. into peritoneal cavity. No symptoms.

G. P. No. 4532. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 11 days prior, inoculated subcutaneously with 0.19 c. c. toxine. No. 7+1 unit antitoxic horse serum (Standard B27).]

14 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. No symptoms.

8 days later, 6 c. c. into peritoneal cavity. Symptoms (?).

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

34 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. Symptoms; recovered.

20 days later, 6 c. c. into peritoneal cavity. Symptoms; recovered.

G. P. No. 4432. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 7 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7.]

22 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. No symptoms.

15 days later, 6 c. c. into peritoneal cavity. Symptoms.

33 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. No symptoms.

21 days later, 6 c. c. into peritoneal cavity. No symptoms.

G. P. No. 4426. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 3 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7.]

27 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. Symptoms (?).

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

34 days later, 6 c. c. into peritoneal cavity. Symptoms.

20 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) in peritoneal cavity. No symptoms.

G. P. No. 4593 Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 3 days prior, inoculated subcutaneously with 0.001 c. c. toxine No. 7.]

18 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. Symptoms.

8 days later, 6 c. c. into peritoneal cavity. Symptoms.

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

34 days later, 6 c. c. into peritoneal cavity. Symptoms.

20 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. No symptoms.

G. P. No. 4377. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 21 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic horse serum (Natl. V. 7).]

Same day, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. Symptoms, less severe.

10 days later, 6 c. c. into peritoneal cavity. No symptoms.

2 days later, 6 c. c. into peritoneal cavity. No symptoms.

15 days later, 6 c. c. into peritoneal cavity. No symptoms.

34 days later, 6 c. c. into peritoneal cavity. No symptoms.

20 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. No symptoms.

G. P. No. 4. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 27 days prior, inoculated subcutaneously with 6 c. c. antitoxic horse serum (Alex. 189).]

3 days later, 6 cc. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. No symptoms.

19 days later, 6 c. c. into peritoneal cavity. Symptoms.

6 days later, 6 c. c. into peritoneal cavity. No symptoms.

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

G. P. No. 4534. Six c. c. antitoxic horse serum (Natl. VIII. 17) injected into the peritoneal cavity. No symptoms.

[Previous treatment: 4 days prior, inoculated subcutaneously with 0.002 c. c. toxine No. 7.]

10 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. No symptoms.

18 days later, 6 c. c. into peritoneal cavity. Symptoms (?).

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

33 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. No symptoms.

21 days later, 6 c. c. into peritoneal cavity. No symptoms.

G. P. No. 2. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. No symptoms.

[Previous treatment: None.]

3 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. No symptoms.

19 days later, 6 c. c. into peritoneal cavity. Symptoms.

6 days later, 6 c. c. into peritoneal cavity. No symptoms.

43 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 18) into peritoneal cavity. Symptoms.

20 days later, 6 c. c. into peritoneal cavity. No symptoms.

G. P. No. 3. Ten c. c. normal horse serum (roan) injected into the peritoneal cavity. No symptoms.

[Previous treatment: None.]

2 days later, 6 c. c. same serum into peritoneal cavity. No symptoms.

3 days later, 6 c. c. antitoxic horse serum (Natl. VIII. 17) into peritoneal cavity. No symptoms.

9 days later, 6 c. c. into peritoneal cavity. No symptoms.

10 days later, 6 c. c. into peritoneal cavity. No symptoms.

PASSIVE IMMUNITY.

EFFECT OF NORMAL GUINEA-PIG BLOOD AND ORGANS UPON THE TOXICITY OF HORSE SERUM.

As a normal untreated guinea pig is entirely insusceptible to the toxic substances found in horse serum, it naturally occurred to us to try to ascertain whether the blood serum or the juices from the various organs of such a normal guinea pig had a restraining, neutralizing, or immunizing action when mixed with horse serum and the mixture inoculated into susceptible guinea pigs.

Normal G. P. A large, full-grown female guinea pig was chloroformed, then exsanguinated. Various organs, mentioned below, were minced and ground separately in a mortar with 10 c. c. of antitoxic horse serum (National VIII. 17). The mixtures were allowed to stand at room temperature 3 hours, then strained through cheese cloth, and injected into the peritoneal cavity of susceptible guinea pigs, as follows:

G. P. No. 4365. Six c. c. of a mixture containing equal parts of antitoxic horse serum and normal guinea-pig serum injected into the peritoneal cavity. Death in 40 minutes.

[Previous treatment: 31 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{350}$ c. c. antitoxic serum (PD&Co. No. 07173).]

G. P. No. 4463. Six c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig liver injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7+ $\frac{1}{200}$ c. c. antitoxic serum (Natl. VIII. 17).]

G. P. No. 4393. Seven c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig liver injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 28 days prior, inoculated subcutaneously with 0.2 c. c. toxine No. 59+1 unit antitoxic serum (Standard B27).]

G. P. No. 4470. Six c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig spleen injected into the peritoneal cavity. No symptoms. For occasional irregularities see below.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic serum (Natl. IX. 17).]

6 c. c. antitoxic horse serum (Natl. VIII. 17) injected into peritoneal cavity of same pig one day later. Symptoms, recovered.

G. P. No. 4475. Six c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig ovary injected into the peritoneal cavity. Death in 45 minutes.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic serum (Natl. IX. 18).]

G. P. No. 4466. Six c. c. of mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig kidney injected into the peritoneal cavity. Death in 45 minutes.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. antitoxic serum (Natl. VIII. 17).]

G. P. No. 4378. Six c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig suprarenal injected into the peritoneal cavity. Death in 10 minutes.

[Previous treatment: 31 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{100}$ c. c. antitoxic serum (Natl. V. 10).]

G. P. No. 4464. Six c. c. of mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig thyroid injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic serum (Natl. VIII. 17).]

G. P. No. 4469. Six c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. VIII. 17) and normal guinea-pig brain injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 26 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic serum (Natl. IX. 17).]

We may conclude from the above that neither the blood serum nor the organs of a normal guinea pig have any neutralizing action upon the toxicity of horse serum when injected into a sensitized guinea pig.

Guinea pig 4470, which received an injection of horse serum plus the spleen pulp of a normal guinea pig, showed no symptoms. We therefore repeated this experiment as follows:

G. P. No. 4493. Six c. c. of a mixture containing equal parts of antitoxic horse serum (Natl. IX. 19) and normal guinea-pig spleen injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 27 days prior, inoculated subcutaneously with 0.19 c. c. toxine No. 7 + 1 unit horse serum (Standard B27).]

We believe that occasional irregularities like this which have exceptionally occurred in this work may be accounted for by the fact that sometimes when the stomach and intestines are full and distended the inoculating needle enters the intestinal tract instead of the peritoneal cavity. While we suspected this possibility, it was proved to our satisfaction one day; after injecting a guinea pig, the intestinal

contents flowed back into the barrel of the syringe, owing to accidental withdrawal of the piston. This particular guinea pig showed no symptoms as a result of the injection; whereas we knew it to be susceptible, because a subsequent operation, done a few hours later, caused characteristic symptoms.

For intraperitoneal inoculations the needle should be short and blunt to avoid this accident and the injection should be given over the region where the coils of small intestine lie close to the abdominal walls.

NEUTRALIZING EFFECT OF THE BLOOD AND ORGANS OF AN IMMUNIZED GUINEA PIG UPON THE TOXICITY OF HORSE SERUM.

We found that repeated injections of horse serum into a guinea pig produces a certain degree of immunity to the subsequent action of horse serum, and it naturally occurred to us to try whether such guinea pigs contained in their body juices an immunizing substance in sufficient quantity to neutralize the poisonous substance found in horse serum.

G. P. No. 109 (immunized). This guinea pig had received 10 subcutaneous inoculations of 1 c. c. each of antitoxic horse serum (Natl. IX. 19) on 10 successive days from Feb. 8 to 20; 15 days later, viz, March 7, it was inoculated with 6 c. c. antitoxic horse serum (Natl. IX. 19) into the peritoneal cavity. No symptoms.

Twenty-one days later, viz, March 28, it was again tested by injecting 6 c. c. of antitoxic horse serum (Natl. VIII. 18) into the peritoneal cavity. No symptoms.

As this guinea pig showed a high degree of resistance to the toxic action of horse serum it was killed two days later, March 30, with chloroform. About 15 c. c. of the blood was taken from the heart and defibrinated, the various organs were removed and placed in separate mortars and ground up with 10 c. c. of antitoxic horse serum (Natl. VIII. 18). This mixture of horse blood with organ juices of the guinea pig was allowed to stand about 3 hours at room temperature and strained through cheese cloth. It was then inoculated into the guinea pig.

G. P. No. 166. Six c. c. antitoxic horse serum (Natl. VIII. 18) mixed with *suprarenal* of g. p. 109 injected into the peritoneal cavity. Dead in 9 minutes.

[Previous treatment: 49 days prior, inoculated with 0.22 c. c. toxine No. 7 + $\frac{1}{300}$ c. c. horse serum (Stearns No. 1351).]

G. P. No. 158. Six c. c. same serum as g. p. 166 mixed with whole (defibrinated) *blood* of g. p. 109 injected into peritoneal cavity. Dead in 15 minutes.

[Previous treatment: As g. p. 166.]

G. P. No. 126. Six c. c. same serum as g. p. 166 mixed with *thyroid* of g. p. 109 injected into peritoneal cavity. Dead in 16 minutes.

[Previous treatment: As g. p. 166.]

G. P. No. 132. Six c. c. same serum as g. p. 166 mixed with *kidney* of g. p. 109 injected into peritoneal cavity. Symptoms, recovered.

[Previous treatment: As g. p. 166.]

G. P. No. 164. Six c. c. same serum as g. p. 166 mixed with *spleen* of g. p. 109 injected into peritoneal cavity. Symptoms, recovered.

[Previous treatment: As g. p. 166.]

G. P. No. 129. Six c. c. same serum as g. p. 166 mixed with *liver* of g. p. 109 injected into peritoneal cavity. No symptoms.

[Previous treatment: As g. p. 166.]

2 hr. 45 min. later. *To test susceptibility.* 6 c. c. same serum as g. p. 166 injected into peritoneal cavity. Dead in 30 minutes.

G. P. No. 147. Six c. c. same serum as g. p. 166 mixed with *brain* of g. p. 109 injected into peritoneal cavity. No symptoms.

[Previous treatment: As g. p. 166.]

1 hr. 20 min. later. *To test susceptibility.* 6 c. c. same serum as g. p. 166 injected into peritoneal cavity. Dead in 35 minutes.

G. P. No. 139 (control). Six c. c. same serum as g. p. 166 injected alone into peritoneal cavity. Dead in 15 minutes.

[Previous treatment: As g. p. 166.]

Owing to the fact that guinea pigs 129 and 147 showed no symptoms, the experiment was repeated, using organs from a similarly treated pig as follows:

G. P. No. 108 (immunized). This guinea pig had received 10 subcutaneous inoculations of 1 c. c. each of normal horse serum (Sam) on 10 successive days from Feb. 8 to 20; 37 days later, viz, March 29, it was inoculated with 6 c. c. antitoxic horse serum (Natl. VIII. 18) into the peritoneal cavity. Symptoms, recovered.

Beginning six days later, viz, April 4, and continuing 12 days, it was given a daily subcutaneous inoculation of 1 c. c. normal horse serum (roan). No symptoms.

Six days after the last inoculation the pig was given 6 c. c. normal horse serum (roan) into the peritoneal cavity. No symptoms.

This guinea pig, having showed a strong resistance to the toxic action of horse serum, was killed with chloroform and the brain, part of the spinal cord, and liver were minced and ground separately in a mortar with 20 c. c. antitoxic horse serum (Natl. VIII. 18). The mixture was allowed to stand about 3 hours at room temperature and strained through cheese cloth and then inoculated.

G. P. No. 4998. Six c. c. antitoxic horse serum (Natl. VIII. 18) mixed with *liver* of g. p. 108 injected into the peritoneal cavity. Dead in 95 minutes.

[Previous treatment: 39 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{8\frac{1}{50}}$ c. c. antitoxic horse serum (Wellcome 474A).]

G. P. No. 5044. Six c. c. antitoxic horse serum (Natl. VIII. 18) mixed with *brain* and portions of the *spinal cord* of g. p. 108 injected into the peritoneal cavity. Dead in 85 minutes.

[Previous treatment: 33 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{8\frac{1}{50}}$ c. c. antitoxic horse serum (NYBH 13C).]

G. P. No. 252. Six c. c. antitoxic horse serum (Natl. VIII. 18) mixed with *brain* and portion of *spinal cord* of g. p. 108 injected into the peritoneal cavity. Symptoms, recovered.

[Previous treatment: 53 days prior, inoculated subcutaneously with $\frac{1}{2\frac{1}{50}}$ c. c. normal horse serum (roan) heated to 60° C. for 30 min.]

G. P. No. 251. Six c. c. antitoxic horse serum (Natl. VIII. 18) mixed with *liver* of g. p. 108 injected into the peritoneal cavity. Symptoms; recovered.

[Previous treatment: 53 days prior, inoculated subcutaneously with $\frac{1}{2\frac{1}{50}}$ c. c. normal horse serum (roan) heated to 60° C. for 30 min.]

As a further proof that the blood serum of an immunized guinea pig can not transfer this immunity, we added such serum from several guinea pigs immunized by repeated injections with normal horse serum; but when this mixture is injected into susceptible pigs they react in a characteristic manner. The experimental data upon this point will be seen in Part IV, page 37, upon the relation of precipitin to the toxic action.

It therefore appears that the "immune bodies," if such exist against the toxic action of horse serum, are not free in the blood and body juices, contrary to the case in diphtheria.

Part X.

FEEDING EXPERIMENTS.

GUINEA PIGS MAY BE SENSITIZED BY FEEDING HORSE SERUM.

Our work up to this point seemed to carry us very far away from an explanation of the cause of sudden death in man following the injection of horse serum. A thorough study of the literature upon this subject discloses the fact that almost all the unfortunate cases of this kind have been due to the first injection of horse serum. If, therefore, man may be sensitized to a toxic principle in horse serum, it must be by some other means than a previous injection of horse serum. We have seen that von Pirquet and Schick, in their studies on serum disease, have actually injected children at intervals of several weeks without any such effect as we have found upon guinea pigs. Further, that on numerous occasions children have been given successive injections of diphtheria antitoxin at intervals of three or four weeks for purposes of immunization.

In casting about for another explanation it occurred to us that probably this action may take place through eating horse meat. We therefore carried on a number of feeding experiments upon guinea pigs. We first fed guinea pigs with normal horse serum by means of a stomach tube, with the following results:

G. P. No. 116. One feeding of 5 c. c. normal horse serum (Jane) into stomach.

27 days later inoculated with 6 c. c. antitoxic horse serum (Natl. IX. 19) into the peritoneal cavity. No symptoms.

G. P. No. 114. Four daily feedings, each of 5 c. c., same serum.

27 days after first feeding and 23 after last, same inoculation as g. p. 116. No symptoms.

G. P. No. 112. Five daily feedings, 5 c. c. each, same serum.

27 days after first feeding and 22 after last, same inoculation as g. p. 116. No symptoms.

G. P. No. 113. Six daily feedings, 5 c. c. each, same serum.

27 days after first feeding and 21 after last, same inoculation as g. p. 116. No symptoms.

G. P. No. 115. Ten daily feedings, 5 c. c. each, same serum.

27 days after first feeding and 15 after last, same inoculation as g. p. 116. Symptoms, recovered.

Only one of these five pigs showed definite and characteristic symptoms following the intrastomachal administration of the horse serum. This pig, No. 115, which was sensitive to the subsequent injections

of horse serum, had received ten feedings of 5 c. c. each of normal horse serum daily. In view of the fact, however, that exceedingly small quantities ($\frac{1}{100000}$ c. c.) of horse serum is sometimes sufficient to sensitize a guinea pig, it seemed to us that feeding animals with a stomach tube might cause slight abrasions, resulting in absorption, so that pigs fed in this manner might really be sensitized through minute wounds of the mucous membrane.

We therefore used another series of pigs and fed the animals without using artificial means. As guinea pigs will not drink horse serum, we found it necessary to dry the serum, reduce it to powder, and then mix it with ground carrots. In this way they took the serum unknowingly with their food. By this means definite amounts of the horse serum may be given and the quantity given to each animal accurately controlled. Half a gram of the dried normal horse serum was thus fed to each pig, which was afterwards tested for susceptibility, as follows:

G. P. No. 4551. Fed 0.5 gm. dried normal horse serum daily from March 15 to 28. Injected March 28 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. IX. 19), 13 days from first and 0 days from last feeding. Symptoms; recovered.

G. P. No. 245. Fed 0.5 gm. dried normal horse serum daily from March 15 to 28. Injected March 28 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. IX. 18), 13 days from first and 0 days from last feeding. No symptoms.

G. P. No. 4581. Fed 0.5 gm. dried normal horse serum daily from March 15 to 29. Injected April 5 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII. 18), 21 days from first and 7 days from last feeding. Symptoms; recovered.

G. P. No. 4540. Fed 0.5 gm. dried normal horse serum daily from March 15 to 31. Injected April 6 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII. 18), 21 days from first and 6 days from last feeding. Symptoms; recovered.

G. P. No. 4546. Do.

G. P. No. 4575. Fed 0.5 gm. dried normal horse serum daily from March 15 to April 6. Injected April 6 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII. 18), 21 days from first and 0 days from last feeding. Symptoms; recovered.

G. P. No. 172. Fed 0.5 gm. dried normal horse serum daily from March 15 to April 5. Injected April 6 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII. 18), 21 days from first and 1 day from last feeding. Symptoms; recovered.

G. P. No. 173. Do.

G. P. No. 276. Fed 0.5 gm. dried normal horse serum daily from March 15 to April 9. Injected April 9 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII. 18), 25 days from first and 0 days from last feeding. Dead in 55 min.

There is no doubt from the above experiments that guinea pigs may be sensitized by feeding to them horse serum. Of the nine pigs so fed in the above series eight reacted to subsequent injections of horse serum, one of these died.

These remarkable results are not surprising when we remember that Uhlenhuth ^a showed the possibility of the intrastomachal immu-

^a Uhlenhuth, —: Neuer Beitrag zum spezifischen Nachweis von Eiereiweiss auf biologischem Wege. Deut. med. Woch., Bd. 26, 1900, p. 734-735.

nization in working on antiproteid immunization. He fed rabbits daily for a number of weeks with egg albumin by means of a stomach tube. The rabbits' serum was examined every eight days. After twenty-four days it developed the power to precipitate egg albumin.

Metchnikoff^a reports that he attained immunization by feeding one animal with the blood of another. He fed horse's blood to white rats. After three or four feedings no agglutination or hemolytic action of the rats' blood upon the horse's corpuscles was noted. In one week the action appeared feeble and increased to decided strength after one or two months.

GUINEA PIGS MAY BE SENSITIZED BY FEEDING HORSE MEAT.

After demonstrating the possibility of rendering guinea pigs susceptible by feeding them with horse serum, we next fed a series with horse meat. The following series was fed with indefinite amounts of horse meat, both fresh and dried ground up with carrots, as guinea pigs do not like fresh horse meat and must be very hungry in order to eat it.

G. P. No. 242. Fed 9 days on horse meat from Feb. 15. Injected March 9 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. IX, 17), 24 days after first and 15 days after last feeding. Symptoms; recovered.

G. P. No. 237. Fed 9 days on horse meat from Feb. 15. Injected March 10 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. IX, 17), 25 days after first and 16 days after last feeding. Symptoms; recovered.

G. P. No. 238. Do.

G. P. No. 239. Do.

G. P. No. 240. Do.

G. P. No. 244. Do.

G. P. No. 241. Fed 9 days on horse meat from Feb. 15. Injected April 5 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 49 days after first and 40 days after last feeding. Symptoms?; recovered.

G. P. No. 243. Fed 9 days on horse meat from Feb. 15. Injected March 13 into peritoneal cavity with 10 c. c. aqueous extract dry horse meat, 26 days after first and 17 days after last feeding. No symptoms.

As the above series was fed with indefinite amounts, another series of guinea pigs was placed upon definite weighed amounts of horse meat. Four grams of the dried ground horse meat were mixed with fresh carrots and fed to the pigs daily. Almost all the pigs placed upon this diet did poorly, their coats became shaggy and the animals lost weight.

G. P. No. 246. Fed 4 gm. dried horse meat daily from March 15 to 28. Injected March 28 with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 13 days after first and 0 day after last feeding. Symptoms?; recovered.

G. P. No. 4562. Do.

^a Metchnikoff, —: Ueber hamolytisches Serum durch Blutfütterung. Centblt. f. Bakt., v. 29, 1901, p. 531-533.

- G. P. No. 4544. Fed 4 gm. dried horse meat daily from March 15 to 29. Injected April 5 with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 21 days after first and 7 days after last feeding. Symptoms; recovered.
- G. P. No. 4543. Fed 4 gm. dried horse meat daily from March 15 to April 6. Injected April 6 with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 21 days after first and 0 day after last feeding. No symptoms.
- G. P. No. 4563. Do. Symptoms?; recovered.
- G. P. No. 4371. Do. No symptoms.
- G. P. No. 270. Do. Symptoms; recovered.
- G. P. No. 4549. Do. No symptoms.
- G. P. No. 4538. Fed 4 gm. dried horse meat daily from March 15 to 31. Injected April 6 with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 21 days after first and 6 days after last feeding. Symptoms; recovered.
- G. P. No. 174. Do. Dead in 20 minutes.
- G. P. No. 275. Fed 4 gm. dried horse meat daily from March 15 to April 9. Injected April 9 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 25 days after first and 0 days after last feeding. No symptoms.
- G. P. No. 4557. Do.
- G. P. No. 4574. Do. Symptoms?; recovered.
- G. P. No. 4569. Do. No symptoms.
- G. P. No. 4566. Do. Symptoms; recovered.

It is perfectly plain from the above that guinea pigs may be sensitized by feeding them horse meat as well as horse serum.

MAY GUINEA PIGS BE SENSITIZED BY FEEDING BEEF?

Another series of experiments was then conducted by feeding guinea pigs with beef. The meat was dried, ground, and mixed in definite weighed amounts with ground carrots.

- G. P. No. 247. Fed 4 gm. dried beef daily from March 15 to 28. Injected March 28 into peritoneal cavity with 5 c. c. antitoxic horse serum (Natl. VIII, 18), 13 days after first and 0 day after last feeding. Symptoms?; recovered.
- G. P. No. 269. Fed 4 gm. dried beef daily from March 15 to 29. Injected April 5 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 21 days after first and 7 days after last feeding. Symptoms?; recovered.
- G. P. No. 171. Fed 4 gm. dried beef daily from March 15 to April 6. Injected April 6 into peritoneal cavity with 6 c. c. antitoxic horse serum (Natl. VIII, 18), 21 days after first and 0 day after last feeding. No symptoms.

Five guinea pigs were placed in this series, but two of them died, apparently as a result of the diet.

We conclude, as a result of these feeding experiments, that guinea pigs may be highly sensitized to the toxic action of horse serum by previous feeding with horse serum or horseflesh. So far as conclusions may be drawn from the few experiments done upon feeding guinea pigs with beef, we feel justified in stating that guinea pigs may also be rendered slightly susceptible in this way. Whether pigs fed with beef would be more susceptible subsequently to the

injection of cattle serum than horse serum is reserved for further study.

The fact that guinea pigs may be rendered susceptible by the feeding of strange proteid matter opens an interesting question as to whether sensitized guinea pigs may also be poisoned by feeding with the same serum. If man can be sensitized in a similar way by the eating of certain proteid substances it may throw light upon those interesting and obscure cases in which the eating of fish and other sea food, etc., by certain individuals habitually causes sudden and sometimes serious symptoms.

Part XI.

HEREDITARY TRANSMISSION OF THE SUSCEPTIBILITY IN GUINEA PIGS.

So far as may be judged from the following data on this subject the susceptibility to the toxic effects of horse serum may be transmitted from the mother guinea pig to her young:

FAMILY NO. 1.

Mother g. p. No. 105. One c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

[Previous treatment: 55 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. normal horse serum (Jane).]

The progeny of the above guinea pig, when about five days old, was tested as follows:

G. P. No. 105A. One c. c. normal horse serum (roan) inoculated subcutaneously. Symptoms; recovered.

G. P. No. 105B. One c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms; recovered.

FAMILY NO. 2.

Mother g. p. No. 66. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Dead in 120 minutes.

[Previous treatment: 85 days prior, 6 c. c. normal horse serum (Sam) injected into the peritoneal cavity.]

The progeny of the above guinea pig, when about a week old, was tested as follows:

G. P. No. 66A. One c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms.

G. P. No. 66B. Do.

FAMILY NO. 3.

Mother g. p. No. 103. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms.

[Previous treatment: 71 days prior, $\frac{1}{250}$ c. c. normal horse serum (Jane) inoculated subcutaneously; 33 days later 6 c. c. antitoxic horse serum (Natl. IX, 17) injected into the peritoneal cavity. Symptoms.]

The progeny of the above guinea pig, when about ten days old, was tested as follows:

G. P. No. 103A. One c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms.

FAMILY NO. 4.

Mother g. p. No. 4463. Six c. c. normal horse serum (roan) injected into the peritoneal cavity. Symptoms (?).

[Previous treatment: 99 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic horse serum (Natl. VIII, 17). 26 days later, 6 c. c. antitoxic horse serum (Natl. VIII, 17) + liver pulp of normal guinea pig injected into the peritoneal cavity. Symptoms.]

The progeny of the above guinea pig, when about ten days old, was tested as follows:

- G. P. No. 4463A. One c. c. normal horse serum (roan) injected into the peritoneal cavity.
Symptoms.
G. P. No. 4463B. Do.

FAMILY NO. 5.

Mother g. p. No. 14. Six c. c. normal horse serum (roan) injected into the peritoneal cavity
Symptoms; recovered.

[Previous treatment: 94 days prior, inoculated subcutaneously with $\frac{1}{250}$ c. c. antitoxic horse serum (Natl. IX, 18.)]

The progeny of the above guinea pig, when five days old, was tested as follows:

- G.P. No. 14A. One c. c. normal horse serum (roan) injected into the peritoneal cavity
Dead in 30 minutes.
G. P. 14B. Do.
G. P. No. 14C. Do. Dead in 35 minutes.

It is plain from the above that young guinea pigs born of a susceptible mother are themselves susceptible, often more so than the mother herself.

To control the effect of horse serum upon such young guinea pigs the following data are given:

(All controls born of normal parents.)

- Control g. p. No. 01. One c. c. normal horse serum (roan) inoculated subcutaneously when 5 days old. No symptoms.
Control g. p. No. 02. Two c. c. same serum when 1 week old. No symptoms.
Control g. p. No. 03. Same injection when 6 days old. No symptoms.
Control g. p. No. 04. Same injection when 4 days old. No symptoms.

These four controls were selected from four different litters.

These results upon the hereditary transmission of the susceptibility to the poisonous action of horse serum in guinea pigs may throw light upon the well-known inherited tendency to tuberculosis in children born of a tuberculous parent.

There are certain analogies between the action of tuberculosis and horse serum. Both produce a hypersensitiveness and also a certain degree of immunity. Now that we have proved that this hypersensitiveness or anaphylactic action in the case of horse serum may be transmitted hereditarily in guinea pigs, may it not throw light upon the fact that tuberculosis "runs in families?" While there are several recorded instances demonstrating that immunity to certain infectious diseases may be transmitted from a mother to her young this is, as far as we know, the first recorded instance in which hypersensitiveness, or anaphylaxis, has been experimentally shown to be hereditarily transmitted from a mother to her young.

Part XII.

TOXIC ACTION OF OTHER ALBUMINOUS SUBSTANCES.

As we found that guinea pigs may be so highly sensitized to the toxic action of horse serum and to a certain extent the serum from other animals we made a few experiments to determine whether other albuminous substances possessed the same toxic properties under these conditions. For this purpose we used egg albumin, peptone, skimmed milk, hemoglobin and vegetable proteid.

G. P. No. 4366. Six c. c. of a saturated solution of egg albumin were injected into the peritoneal cavity. No symptoms.

[Previous treatment: 30 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{400}$ c. c. horse serum (PD & Co. 08022-A)].

Two days later this guinea pig was tested for susceptibility by the inoculation of 6 c. c. antitoxic horse serum (Natl. VIII. 17) into the peritoneal cavity. Dead in 50 minutes.

G. P. No. 4924. Six c. c. of a saturated solution of peptone injected into the peritoneal cavity. No symptoms.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{300}$ c. c. antitoxic horse serum (Cutter 1540)].

Three days later this guinea pig was tested for susceptibility by the inoculation of 6 c. c. antitoxic horse serum (Natl. IX. 17) into the peritoneal cavity. Symptoms; recovered.

G. P. No. 4926. Six c. c. skimmed milk injected into the peritoneal cavity. No symptoms.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{400}$ c. c. antitoxic horse serum (Cutter 1540)].

Three days later tested for susceptibility by the injection of 6 c. c. antitoxic horse serum (Natl. IX. 17) into the peritoneal cavity. Dead in 11 minutes.

G. P. No. 4919. Ten c. c. vegetable proteid from oats injected into the peritoneal cavity. No symptoms.

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{200}$ c. c. antitoxic horse serum (Stearns 16 H)].

Three days later tested for susceptibility by the injection of 6 c. c. antitoxic horse serum (Natl. IX. 17) into the peritoneal cavity. Dead in 25 minutes.

G. P. No. 4925. Six c. c. hemoglobin solution in water from washed normal (roan horse) corpuscles injected into the peritoneal cavity. No symptoms (?)

[Previous treatment: 40 days prior, inoculated subcutaneously with 0.139 c. c. toxine No. 5 + $\frac{1}{300}$ c. c. antitoxic horse serum (Cutter 1540)].

Three days later tested for susceptibility by the injection of 6 c. c. antitoxic horse serum (Natl. IX. 17) into the peritoneal cavity. Symptoms; recovered.

G. P. (normal). Four and a half c. c. solution of hemoglobin (watery solution of washed red blood corpuscles of roan horse) injected into peritoneal cavity. No symptoms.

G. P. No. 4989. Ten c. c. same injection. Symptoms (?)

[Previous treatment: 25 days prior, inoculated subcutaneously with 0.22 c. c. toxine No. 7 + $\frac{1}{200}$ c. c. antitoxic horse serum (Alex. A202)].

To control the two preceding pigs a solution of hemoglobin, obtained by dissolving red blood corpuscles from a normal horse (roan), was injected into the peritoneal cavity of a normal guinea pig, with negative results.

Whether guinea pigs treated with these albuminous substances are rendered susceptible to subsequent injections of the same albumin is now being studied.

Part XIII.

A REVIEW OF THE LITERATURE RELATING TO OUR WORK.

We feel it incumbent upon us to compare our results with the work of others and, therefore, have introduced this discussion upon the toxic action of serums in general, especially in relation to the production of immunity and hypersensitiveness.

NOTE.—In this historical development we have drawn largely upon the splendid review of the literature as given by Uhlenhuth in "Zur Kenntniss der giftigen Eigenschaften des Blutserums" (Zeit. f. Hyg., v. 26, 1897), and C. Frh. von Pirquet and B. Schick in "Die Serumkrankheit" (K. K. Universitäts-Kinder-Klinik, Wien, 1905).

Transfusion was formerly used as a therapeutic measure. The first reference to this practice is June 15, 1667, when von Denis transfused lamb's blood (cited in Landois's article on transfusion, Eulenburg's Realenzyklopädie, 3. Auflage). This practice gradually fell into disuse but was again revived about the beginning of the last century, when transfusion was used for acute anemia and poisonings.

The intravenous injection of lamb's blood was soon shown to be associated with great danger. High fever in half an hour, emboli, hemorrhages, hemoglobinuria, etc., were often noticed. The causes of these serious symptoms, as well as the scientific basis of our knowledge upon the effects of transfusion, were first made clear by the work of Landois and Ponfick in the years 1873 and 1875. These authors showed that the blood of alien species caused solution of the corpuscles when brought into the circulation. Naunyn and Francken showed that the injection of dissolved hemoglobin into the circulation caused coagulation. Great numbers of the white corpuscles were so acted upon by the dissolved hemoglobin that the fibrin-forming elements were thus set free, resulting in the formation of clots within the vessels. When this coagulation is extensive, death may result from asphyxia.

Dallera ^a in 1874 reported that urticarial eruptions may follow the transfusion of blood.

^a Dallera: Considerazioni e casi clinici di transfusione del sangue. Il morgagni, 1874, 7.

Neudörfer ^a refers to the fact that urticaria frequently follows transfusion.

Landois ^b also refers to this complication.

In consequence of the severe injury which often resulted from the transfusion of lamb's blood the practice was entirely discontinued. Recently, however, Dominici ^c has again taken up the subject.

In England at one time the transfusion of milk was practiced, but proved dangerous and without benefit, as stated by Montard, Martin, and Richet. (Injections intraveineuses de lait et de sucre, Soc. de Biol., 1879.)

Latterly the transfusion of lamb's blood has given place to physiological salt solution and also to the transfusion of defibrinated human blood.

In the year 1894 the use of diphtheria antitoxin introduced the widespread practice of injecting horse serum. This practice differed from the previous work with transfusion in that the injections are generally not given intravenously, but subcutaneously, and the quantity of the alien albuminous substance is relatively small. According to von Pirquet and Schick this accounts partly for the fact that in the majority of these injections no injurious consequences followed. Luebinski (Über eine Nachwirkung des Antitoxins bei Behandlung des Diphtherie, Deut. med. Woch., 1894) was the first to call attention to a case of exanthematous eruption following the injection of antitoxin serum. Soon afterwards Schütz, ^d Cnyrim, ^e Asch, ^f Rembold, ^g and Trey mann ^h reported urticarial eruptions following the prophylactic injection of antitoxic horse serum. Following these came a great mass of evidence which made it clear that following the injection of antidiphtheric serum these sequelæ were comparatively harmless.

In relation to the cause of these symptoms it was generally held that the serum contained some toxic substance, probably a globulin. This explanation led manufacturers to the commendable practice of starving their horses about twenty-four hours prior to bleeding, in order to eliminate as far as practicable the freshly assimilated products of digestion.

^a Neudörfer: Beiträge zur Bluttransfusion. Zeitschr. f. Chirurgie, Bd. 6.

^b Landois: Die Transfusion des Blutes, Leipzig, 1875. —: Transfusion. Eulenburg's Realencyclopädie, 3. Aufl., 1900.

^c Dominici: Transfusion. Wiener med. Wochenschr., 1895.

^d Schütz: Discussionsbemerkung zu Piorkowski's Vorträge. Berl. med. Gesellsch., 1904.

^e Cnyrim: Zwei Fälle von Erkrankungen nach Anwendung des Diphtherieserums. Deut. med. Woch., 1894, p. 898.

^f Asch: Zur Casuistik der Heilserumexantheme. Berl. klin. Woch., 1894.

^g Rembold: Zwei Fälle von Erkrankung nach Anwendung des Heilserums. Deut. med. Woch., 1894, p. 963.

^h Trey mann, Otto: Ein Fall von acuter hämorrhagischer Nephritis nach Anwendung des Behring'schen Diphtherieheilserums. Deut. med. Woch., 1894, p. 952.

Heubner ^a and von Bókay ^b expressed the opinion that these manifestations were due to other properties than the antitoxin in the serum.

Johannessen ^c believed that the agent in horse serum which produced these symptoms was due to the introduction into the body of an alien serum, for he produced the same effects by injecting normal horse serum. In 22 cases fever resulted, and skin eruptions in 12.

Sévestre ^d referred the exanthems which appear in eight to ten days back to the serum which had been injected. However, he thought that the measles-like eruption and fever was the expression of a streptococcus infection. Netter, however, in the discussion, believed these symptoms to be caused by the serum.

Almost all authors express the opinion that the symptoms caused by the injection of serum are of minor consequence. The fact that from time to time serious symptoms and even death followed the injection of diphtheria antitoxic serum does not alter the general impression that as a rule such injections are harmless. *The benefits far outweigh the danger.*

Gottstein, ^e in addition to the Langerhans' case, collected 8 deaths following the injection of serum in those having diphtheria and 4 in those not sick with diphtheria.

We have collected from the literature 19 cases of such unfortunate results, and know personally of several more which have not been reported. Von Pirquet and Schick express the opinion that a critical examination of these cases may be otherwise explained, and authors generally have not permitted this rare accident to counterbalance the great benefit possible from the use of diphtheria antitoxic serum.

It seems to have been definitely shown that the skin eruptions and other symptoms following the injection of horse serum follow in direct proportion to the amount of serum injected. This has resulted in endeavors to concentrate the serum as much as possible.

^a Heubner: Praktische Winke zur Behandlung der Diphtherie mit Heilserum. Deut. med. Woch., 1894, p. 701. — Klinische Studien über die Behandlung der Diphtherie mit dem Behring'schen Heilserum. Leipzig, 1895. — Über die Anwendung des Heilserums bei der Diphtherie. Jahrb. f. Kdheilk., Bd. 38, p. 231.

^b Von Bókay: Die Heilserumbehandlung gegen Diphtherie im Budapeste Stefanie-Kinderspital. H. f. Kdh., Bd. 44, 1897. — Meine Erfolge mit Behring's Diphtherieheilserum. Deut. med. Woch., 1895, p. 233. — Meine Erfahrungen mit dem Moser'schen polyvalenten Scharlach-Streptokokkenserum. Deut. med. Woch., 1904.

^c Johannessen: Über Injektionen mit antidiphtherischen Serum und reinem Pferdeserum. Deut. med. Woch., 1895. — Über Immunisierung bei Diphtherie. Deut. med. Woch., 1895.

^d Sévestre: Des accidents causés par le streptococque à la suite des injections de sérum de Roux. Bull. de la Soc. méd. des hôpitaux, July 19, 1895, Jan. 31, 1896. La méd. moderne, 1896.

^e Gottstein: Über Todesfälle, welche bei der Anwendung des Diphtherieheilserums beobachtet worden sind. Therap. Monatsh., 1896.

Bujwid ^a believed that these manifestations were due largely to fresh horse serum, and favors the use of old seasoned antitoxin for therapeutic purposes.

Hamburger and Moro ^b have shown that the injection of alien serums into man result in the formation of precipitins.

Hamburger, ^c in a further work, drew a distinction between alien albuminous substances introduced through the digestive tract and by other channels.

Upon the general toxic properties of blood we quote the following instances, taken largely from Uhlenhuth: ^d

Stern, ^e 1893, found that the blood from a case of erysipelas in amounts of 0.5 to 1 c. c. killed white mice, while normal human blood required 3 c. c. or more to kill the animals.

Rummo, ^f 1891, showed that blood serum from cases of typhoid fever, malaria, pneumonia, and eclampsia had a high grade of toxicity for rabbits when injected intravenously.

Albu, ^g 1897, confirm Rummo's experiments, and found an increase of toxicity in persons suffering from pneumonia, severe chronic bronchitis, epilepsy, uræmia, and puerperal sepsis.

Upon the toxicity of the blood serum of man in health and disease further work has been done by Charrin, ^h Leclainche and Rémond, ⁱ Chambrelent and Tarnier, ^j Ludwig and Savor, ^k Guinard and Dumarest. ^l

^a Bujwid, O.: Kann des Antidiphtherieserum schädlich sein? Polnisch, ref. Virchow's Jarhb., 1897, II, p. 659.

^b Hamburger, F., and Moro: Über die biologischen nachweisbaren Veränderungen des menschlichen Blutes nach Seruminjektion. Wiener klin. Woch., 1903.

^c Hamburger, F.: Zur Frage der Immunisierung gegen Eiweiss. Wiener klin. Woch., 1902. —: Arteigenheit und Assimilation. Wien, 1903.

^d Uhlenhuth: Zur Kenntniss der giftigen Eigenschaften des Blutserums. Zeit. f. Hyg., vol. 26, 1897, p. 384.

^e Stern: Ueber einige Beziehungen zwischen menschlichen Blutserum und pathogenen Bakterien. (XII Congress für innere Medicin, Wiesbaden, 1893): Deut. med. Woch., 1893.

^f Rummo: Ueber die Giftigkeit des Blutserums bei Menschen und Thieren im normalen Zustande und bei Infectiouskrankheiten. Wiener med. Woch., 1891.

^g Albu: Untersuchungen über die Toxicität normaler u. pathol. Serumflüssigkeit. Virchow's Archiv., bd. 140, 1897.

^h Charrin: Compt. rend. soc. biol., 1890.

ⁱ Leclainche and Rémond: Compt. rend. soc. biol., 1890, p. 1037.

^j Ludwig and Savor: Monatschrift für Geburtshilfe, bd. 1, 1895.

^k Tarnier and Chambrelent: Note relative à la recherche de la toxicité du sérum sanguin dans deux cas d'éclampsie puerpérale. Soc. de biol., 1892.

^l Guinard and Dumarest: Note sur la détermination de la toxicité du sérum sanguin: Techniques et résultats. Compt. rend., 1897, No. 15. Variations de la toxicité du sérum sanguin dans certaines infections expérimentales. Loc. cit., No. 18. A propos de la détermination physiologique et clinique de la toxicité du sérum humain. Loc. cit., No. 18.

Bar and Rénon,^a Picolini and Conti,^b Mairét and Bosc.^c All of these authors determined the toxicity of the blood serum in accordance with Rummo's method of intravenous injections into rabbits.

The poisonous properties of the blood serum from healthy men, according to the work of these authors, varies considerably, as may be judged from the following summary:

Rummo found 10 c. c. as the fatal dose for 1 kilogram of rabbit.

Lugwig and Savor, 8 to 9 c. c.

Chambrelent and Tarnier, 10 c. c.

Albu, 9.5 to 11 c. c.

Mairét and Bosc, 12.5 to 18.0 c. c.

Guinard and Dumarest, 17 c. c.

Leclainche and Rémond, 23 c. c.

Charrin, 27 c. c.

It will therefore be seen that the fatal dose of normal human serum, according to these different investigations, varies between 8 c. c. and 27 c. c. per kilogram of rabbit.

Uhlenhuth found that the intravenous injection of from 7 to 10 c. c. of normal blood serum per kilogram of rabbit regularly caused death within one-half hour.

The blood serum of other animals was injected intravenously into rabbits and showed considerable differences in their toxicity. The quantity necessary to kill in proportion of 1 kilogram of rabbit was:

	c.c.
Sheep serum	11
Hog serum	12
Cattle serum	6

Horse serum on the other hand, when injected in such large quantities as 60 c. c. and more per 1 kilogram of rabbit, not only did not kill but caused no reaction at all.

In 1888 Mosso^d discovered that eel serum in doses as small as 0.02 c. c. per 1 kilogram of rabbit caused death.

Uhlenhuth, finding intravenous injections into rabbits unsatisfactory, used subcutaneous inoculations into guinea pigs. He found that the injection of small quantities (0.5 c. c.) of human,

^a Bar and Rénon: De la toxicité du sang et de l'urine chez une femme atteinte de troubles gravido-cardiaques. Compt. rend. soc. biol., 1894.

^b Picolini and Conti: Toxicité du sérum sanguin et de l'urine dans la pneumonie.

^c Mairét and Bosc: Recherches sur les causes de la toxicité du sérum du sang. Compt. rend., v. 119, p. 292. Toxicité du sérum du sang de l'homme sain. Comp. rend., 1897. *Des effets de la chaleur sur la toxicité du sérum. Compt. rend., 1894.

^d Mosso: Die giftige wirkung des serums der muraeniden. Arch. f. exper. pathol. u. pharmakol., bd. 25, p. 111.

sheep, hog, and rabbit serums caused infiltration, and of large quantities (15 to 20 c. c.) necrosis. On the other hand, cattle serum caused death in doses of 10 to 15 c. c., while horse serum in doses of 20 c. c. caused no infiltration and in larger doses a very slight infiltration which entirely disappeared within forty-eight hours.

Pfeiffer^a confirmed Uhlenhuth's findings and believed that the necrotic action was due to a "haptin" substance identical with the hemolytic action of blood serum.

Von Pirquet and Schick, in their work on "Die Serumkrankheit," have developed the clinical manifestations following the injection of horse serum in man into a syndrome which they call "the serum disease." The principal manifestations of this disease are a period of incubation varying from eight to thirteen days, fever, skin eruptions, swelling of the lymph glands, leukonemia, joint symptoms, edema and albuminuria.

The following historical development of this phase of the subject, which bears such a close relation to our work, is largely a free translation of von Pirquet and Schick's monograph.

As a result of their studies von Pirquet and Schick consider their most important conclusions to be the fact that the power of reaction in serum disease may show itself either immediately or after a shortened period of incubation.

Arthus^b described hypersensitiveness and explained its significance with special reference to the serum disease. He based his work upon that of Richet,^c who showed in his experiments upon actinia poison (the actinia is a sea anemone) that the first injection causes death in dogs in doses between 0.2 and 0.18 gram per kilogram of body weight. In no case does death occur before ten hours. Upon subsequent injection the animal died from smaller doses (0.15 gm.) and much more quickly. These injections were all intravenous. The following is a characteristic example: A dog receives the first time 0.1 gm. of the actinia poison per kilogram of his body weight, from which it shows scarcely perceptible symptoms. After twenty-two days the dog was again injected with 0.1 gm. per kilogram of weight in the saphenous vein. Several seconds later the dog developed coughing respiration and could hardly drag itself along, lay upon its side, bowels evacuated, bloody vomiting, and died in twenty-five minutes. Richet extracted two different bodies from the

^a Pfeiffer, Hermann: Ueber die nekrotisirende Wirkung normaler Seren. Zeit.f. Hyg., Bd. 51, 1905, p. 183.

^b Arthus: Injections répétées de sérum de cheval chez le lapin. Compt. rend., 1903.

^c Richet: De l'anaphylaxie, ou sensibilité croissante des organismes à des doses successives de poison. Arch. di fisiol., 1904, p. 129. — De l'action de la congestine sur les lapins et de ses effets anaphylactique. Compt. rend. Soc. biol., Jan. 21, 1905. — De l'anaphylaxie après injections de congestine chez le chien. Compt. rend. Soc. biol., 1905.

actinia poison: The crystalline *thallassin*, which had slight toxic action, but which in minimal doses caused pruritis, and *congestin*, an albuminous body which was more toxic than the original substance and caused the characteristic congestive conditions in the intestinal tract.

Richet made further experiments with the congestin with relation to first and subsequent injections which gave him the same results as similar experiments with the actinia poison. The fatal dose for rabbits was 0.009 gm. per kilogram for the first injection; for the subsequent injection it was less than 0.0033. Richet designated this hypersensitiveness, caused by the first injection, by the term "anaphylactic" in contradistinction to prophylactic. This anaphylaxis requires for its development a certain time. Three to four days after the first injection there is no hypersensitiveness. It continues a very long time and is still evident after one year. He did not succeed in transmitting this hypersensitiveness by means of the serum of injected animals. He calls attention to similar phenomena in tuberculosis and tetanus.

Knorr,^a as also Behring and Kitashima,^b found that guinea pigs develop an increasing sensitiveness against tetanus toxin.

Serum and actinia poison are similar in that they are not substances capable of self-multiplication. On the other hand, there is this important difference between the two: The actinia poison causes after the first injection symptoms without a period of incubation, while the serum, even in the largest quantities, at the first injection almost without exception develops no immediate symptoms.

So far as serum is concerned, we may assert that the same is not toxic in itself, but that the toxic body is developed through the reaction between the organism and the antibodies.

Similar to serum are forms of animal albuminous substances as, for example, milk (Arthus) and spermatozoa (Wolff).

Entirely analogous to the actinia poison is the hypersensitiveness found in tuberculosis. The question in tuberculosis has been more closely studied in its relation to hypersensitiveness; another well-known fact is that in addition there also develops an immunity.

Tuberculin is an extract which lacks the power of self-multiplication, but is derived from an agent which has this power, and we would expect that infection with the tubercle bacillus would also carry the power of producing this hypersensitiveness the same as is produced by the extract from dead tubercle bacilli.

^a Knorr: Experimentelle Untersuchungen über die Grenzen der Heilungsmöglichkeit des Tetanus. v. 102, 18.

^b Von Behring and Kitashima: Über Verminderung und Steigerung der ererbten Giftempfindlichkeit. Berl. klin. Woch., 1901, p. 157.

Here we come to speak of hypersensitiveness in infectious processes. Arloing, in 1888, stated as his opinion that the pathogenic organisms, above all the tubercle bacilli, excrete soluble substances that influence the organism in such a way that the animal at a later infection with the same bacilli dies more quickly.

Courmont^a studied this question in relation to the tubercle bacillus. He found that bacilli obtained in pure culture from tuberculous pleurisy caused in rabbits general tuberculosis and kill guinea pigs without microscopic lesions. He injected animals with the filtered soluble products of young cultures of this bacillus.

Guinea pigs and rabbits never react to these injections. However, if the animals so prepared were immediately afterwards inoculated with pure cultures then they reacted, as did the untreated animals; but if the inoculation follows several days after the introduction of the soluble products, then the results were very different. Animals which twenty days previously had been injected with the filtrate, as a result of which they showed no reaction, were then inoculated with a tubercule from a guinea pig; then the guinea pigs died in fifteen and the rabbits in about twenty-three hours. The animals died sixteen times more quickly than the control animals. This predisposition seems to be at its height from four to twenty days after the first injection of the soluble extract. Courmont believes that the organism, as a result of the previous treatment, becomes a better culture medium for the infection. The gist of his explanation lies in the fact that the organism possesses for itself protective substances which are eliminated or neutralized by means of the soluble products of the first injection. This explanation is called, for short, the "absorption theory" (Ausschaltungs Theorie). Why several days are necessary for this action Courmont does not explain.

The school at Lyons developed this observation in relation to other micro-organisms, as the staphylococcus, streptococcus, bacillus pyocyaneus, etc. Rist made similar observations with the diphtheria bacillus.

Strauss and Gamaleia^b report that animals, after repeated injections with dead tubercle bacilli, die acutely. They bear the first injection of large quantities without reaction.

Babes and Proca^c confirmed this observation.

Against the "addition" theory of Koch, to which most of the German authorities adhere, and against the "absorption" theory of the

^a Courmont: Études sur les substances solubles prédisposantes à l'action pathogène de leurs microbes producteurs. Rev. de méd., 1891. Centbl. f. Bakt., Bd. 13, p. 714.

^b Strauss, L., and N. Gamaleia: Recherches expérimentales sur la tuberculose. Arch. de méd. expériment., III, 1899.

^c Babes and Proca: Untersuchungen über die Wirkung der Tuberkelbacillen und über gegenwirkende Substanzen. Zeit. f. hyg., v. 23, p. 331.

Lyons school, Köhler and Westpfal^a in 1891 announced a third theory to explain the action of tuberculin. The last-named authors believed that, through the union of tuberculin with the products of the tubercle bacilli in the tuberculous lesions, a third and new body results which causes the clinical manifestations of the tubercle reaction.

A similar explanation is used by Marmorek to account for the elevation of temperature. He believes that the tubercle bacilli, under the influence of tuberculin, secrete a pathogenic substance.

Bail, based upon the work of Detre-Deutsch, has taken up anew the work of Courmont and studied more precisely the hypersensibility in tuberculosis. To explain this hypersensibility in tuberculous guinea pigs he advances another theory, based upon the power to transmit the hypersensibility. For example, if we inject an animal, into the peritoneal cavity, at a certain stage of tuberculosis the animal dies rapidly. At the site of the injection an exudate is produced. If this exudate is added to tubercle bacilli and injected into normal animals it produces sudden death.^b

Bail believes that the tubercle bacillus secretes a soluble substance in the infected organism which substance exerts a paralytic action upon the leucocytes. This substance he has called "aggressin." He believes that the exudate obtained by this reaction contains this aggressin and, when carried over, has the power of destroying the power of the leucocytes—that is, the protecting power of the new organism—and therefore the poisonous substance in the tubercle bacillus is able to develop its power quickly.

This explanation seems to be in line with Arloing and Courmont's.

In recent years Wolff^c has also worked up the question of hypersensibility, proceeding upon the work of Pfeiffer upon the endotoxins. The endotoxin only possesses power when the bacterial capsules are dissolved by means of bacteriolysins that are freed by means of antibodies. As soon as the endotoxin is set free it exerts its power and, without a period of incubation, is a powerful poison.

The results of Pfeiffer and Wolff's observations upon the method of operation of the endotoxin are very closely related to von Pirquet and Schick's explanation of the production of the serum disease.

Wolff also experimented upon the question of hypersensibility caused by the reinjection of dissolved albuminous substances and his observations coincided with those of Arthus, Pirquet, and Schick. The endotoxic theory, in the sense of bacteriolysis, naturally can not

^a Köhler and Westpfal: Eine neue Theorie zur Erklärung der Wirkung des Koch'schen Heilmittels auf den tuberculösen Menschen. Deut. med. woch., 1891, p. 839.

^b Bail: Ueber Empfindlichkeit bei tuberculösen Thieren. Wiener klin. woch., 1904. — Der acute Tod von Meerschweinchen an Tuberculose. Loc. cit., 1905.

^c Wolff, A.: Über grundgesetze der immunität. Centblt. f. bakt., bd. 37, 1904, pp. 390, 566, and 684.

be applied to albuminous substances in solution. We can only accept it in the sense that by means of the reaction between the antibodies and the antigen the poisonous substance is formed.

When it is necessary to conceive of bacteriolytic antibodies to produce solution in order to cause a reaction we must remember that the production requires a definite period of time. This led to the question of the cause of the period of incubation, the significance of which is important.

The long incubation period in tetanus, as has been demonstrated, may be explained by the fact that tetanus poison has a long distance to go along the nerve route before it comes into contact with the susceptible cells.

In the case of malaria the interval between the two paroxysms is explained by the fact that the symptoms of the disease are produced as a result of the particular phase in the developmental cycle of the parasite.

We have a similar conception of the incubation period of a number of diseases, for example, measles, smallpox, etc., in which we look upon the period of incubation as due to a breeding of the causative factor of the disease.

All of the above theories which account for the period of incubation of disease explain this phenomenon by referring it wholly and solely to the parasite and its metabolic products and do not take into account the factor of the infected organism. Pfeiffer and Wolff, however, in explaining the incubation period in infectious processes, take this factor into account: The rôle which the organism plays in the period of incubation in the infectious process becomes clearer from the studies upon the power of serum to produce a reaction.

Von Pirquet believes that, in his work on the hastening power of reaction in the case of vaccinia, the power which the organism plays in the period of incubation is very evident.

While the general reaction following the first vaccination at the very earliest occurs on the seventh day, it appears earlier upon revaccination. Also, the course of the reaction is changed in the sense of a decidedly shortening and weakening of the symptoms. The earlier the reaction appears the weaker does the whole process result.

How can we explain these phenomena? If we use the theories generally in vogue, that the cause of the infection must first multiply to certain numbers in order to be able to produce symptoms, we must believe that the cause of the infection develops more quickly and in larger numbers in the animal which has been previously treated than in the normal animal. We have already inferred that Arloing has suggested this possibility.

On the other hand, we must take into account that in tuberculosis and vaccinia, no matter how much of the causes of these infections

we may introduce, it is not possible to shorten the period of incubation. Beclère, Chambon and Ménard^a have shown that, in the vaccination of calves, the eruption does not appear sooner if the calf is very heavily treated with the vaccinal material.

We might attribute the phenomena to the virulence of the infecting organisms, but the same lymph causes the reaction to appear in animals primarily vaccinated in the normal period of incubation; whereas in those revaccinated there is a hastened reaction.

A related thought originated with Buttersack^b in regard to infectious diseases who, in a study upon recovery and immunity, asserts that recovery is due to a retardation of the development of the cause of the infection at the height of the sickness. He believes further that the cells of the body, through use in the sense of Darwin's theory of evolution and adaptation, develop the power to combat more quickly the multiplication of a new infection.

Von Pirquet and Schick draw this distinction between Buttersack's theory and their own: Buttersack places this power of the organism to prevent a further development of the infection at the climax of the disease, while they believe the antibodies are formed at the very beginning. Their conception of antibodies does not coincide precisely with the generally accepted idea of antibodies, but they use this expression in a general sense to comprise the sum of all the specific reaction products produced by the organism which are able to react upon the antigens introduced. Buttersack's theory does not cover the explanation of the serum disease, as serum has no power of self-multiplication.

The sooner the reaction in the organism succeeds, the less time has the alien infection to develop. Therefore, its development is restricted earlier and, in consequence, the whole organism suffers less damage.

On the contrary, in the case of serum disease we receive the impression that it is unfavorable for the organism to react more quickly to the reagent. For the quicker the antibodies unite with the antigens the more severe will the disease be.

This contradiction may perhaps be cleared up when we remember that the subcutaneous injection of an agent incapable of self-multiplication seldom occurs in nature (insect bites, snake poison) and that this to a certain extent represents an artificially produced form of disease. The natural way for disease to be produced is, in the great majority of cases, by the introduction of minute quantities of an irritant capable of self-multiplication.

^a Beclère, Chambon, and Ménard: *Étude expérimentale des accidents postsérothérapiques*. Ann. de l'Inst. Pasteur, 1896. — *Études sur l'immunité vaccinale*. Ann. de l'Inst. Pasteur, 1896 and 1899.

^b Buttersack: *Immunität und Heilung im Lichte der Physiologie und Biologie*. Virchow's Arch., Bd. 142, p. 248.

The hastening power of the reaction must be regarded as an advantage that the organism has won for itself through the occurrence of the first disease.

In applying this view to disease von Pirquet and Schick find that an organism in the stage of the free antibodies is an expression of the immediate power of reaction or hypersensitiveness. This stage has only a limited duration. The free antibodies disappear; however, the individual remains immune. The fact of this immunity consists, however, no longer in the power of immediate reaction against the cause of the infection, but in a hastened power of reproduction of antibodies. An organism has the power to combat a newly introduced infection and localize it, as is well shown in the case of vaccination. Von Pirquet and Schick believe that this property does not depend so much upon free antibodies in the fluids as upon a property acquired by the cells through the first disease, in which we see an expression of cellular immunity.

In Wassermann's^a observation that the adaptation of the tissues to the existence of microorganisms which were naturally pathogenic without any apparent reaction and production of antibodies we see an instance of immunity through insusceptibility.

A series of diseases—for example, smallpox, measles, varicella, rötthlen—cause after one attack the individual to remain more or less protected throughout the rest of his life. They have the common clinical characteristic that, after a long and definite period of incubation, the disease runs a course in a definite and comparatively short time. If the organism does not die as a result of the disease, then it has won a complete victory over the cause of infection; the same is no longer able to produce harm in such an organism.

According to von Pirquet and Schick the fact that the clinical immunity against this group of diseases, for which we may take vaccinia as a type, does not consist of an acquired nonsusceptibility against the cause of the infection, but the power of an accelerated reaction. They believe they have shown from their work that they have reawakened interest in the serum disease and that this syndrome is not only of interest clinically but, from the standpoint of general pathology, is of the greatest importance.

Our explanation of the cause of sudden death following the second injection of horse serum does not differ essentially from the theory (which has just come to our notice as our manuscript is being edited for press) published by von Pirquet and Schick, relative to the reaction of the serum disease in man, although these similar deductions were reached independently and from different premises.

^a Wassermann, A.: *Über natürliche und künstliche Immunität*. Zeit. f. Hyg., bd. 37, p. 173. — *Wesen der Infection*, in Kolle und Wassermann. Handb. der pathogen. Mikroorganismen, 1903.

We believe that the substance which sensitizes the animal is identical with that which later poisons it, absurd as that may seem at first glance. However, the first substance must cause a reaction in the organism resulting in the production of "antibodies" and it is these antibodies combining with a substance in the horse serum that produce the toxic action. We have found that small quantities of serum produce, after a definite period of incubation, a condition of anaphylaxis. Large quantities probably produce a lesser grade of hypersusceptibility. Multiple or repeated injections produce immunity. We therefore possess in horse serum a substance capable of causing both anaphylaxis and prophylaxis.

SUMMARY AND CONCLUSIONS.

Normal horse serum, when injected into the peritoneal cavity of a normal guinea pig, produces no symptoms. When injected subcutaneously there may result at most a slight local reaction consisting of swelling and edema, which gradually disappears.

Antitoxic horse serum is equally harmless for normal guinea pigs.

Horse serum is, however, poisonous to a guinea pig which has previously been injected with horse serum. The "period of incubation" or time necessary to elapse between the first and second injection is about ten days. Under these circumstances, horse serum is poisonous whether injected subcutaneously or into the peritoneal cavity.

The first injection of horse serum renders the guinea pig susceptible.

The symptoms caused by the injection of horse serum into a susceptible guinea pig are respiratory embarrassment, paralysis, and convulsions, followed by death. The symptoms come on usually within ten minutes after the injection, and when death results it usually occurs within one hour, frequently in less than thirty minutes, and sometimes within a few minutes.

The poisonous principle in horse serum appears to act upon the respiratory centers. The heart continues to beat long after respiration ceases.

The toxic action of horse serum bears no relation to diphtheria. The poison is not *toxone*. Guinea pigs can not be rendered susceptible by previous infections with the *B. diphtheriæ* or by previous injections with diphtheria toxine.

It seems from our work, however, that guinea pigs first injected with a mixture of diphtheria toxine plus horse serum are more sensitive to subsequent injections of horse serum than are guinea pigs sensitized with a first injection of horse serum alone.

DIPHTHERIA ANTITOXIN PLAYS NO PART IN THIS POISONOUS ACTION AND IN ITSELF IS HARMLESS.

As soon as we realized that the toxic principle in horse serum exerts its action in quantities so minute as to place it almost in the category of the ferments and, further, when we concluded from our work that this toxic principle is doubtless one of those highly organized and complex proteid substances belonging to the "haptin group" in the sense used by Ehrlich, we recognized how futile it would be with present methods to attempt to isolate this substance.

Nevertheless we devoted much time and study to the relation of this toxic principle to various chemical, physical, and electrical influences. The practical importance of eliminating or neutralizing this toxic principle in horse serum is at once evident.

It is probable that when the strange proteid is introduced into the guinea pig it causes a reaction resulting in a production of "antibodies," so that when a second injection of horse serum is given there is probably either a union or a reaction between the antibodies and a substance in the horse serum which produces the poisonous effect.

This poisonous principle is quantitatively specific; that is, guinea pigs treated with horse serum are rendered somewhat susceptible to the subsequent injection of the serum of another animal. Guinea pigs treated with the serum of another animal are slightly sensitive to the toxic action of horse serum.

Guinea pigs treated with the serums of various animals and subsequently injected, are much more susceptible to homologous serums than to heterologous serums.

This poisonous action has no relation to hemolysis. Our work proves that blood serum may contain an acute poison entirely independent of any hemolytic action. Normal horse serum has no lytic power upon the red corpuscles of the normal guinea pig.

This poisonous action has no relation to the specific albuminous precipitins.

The poisonous principle in horse serum is not affected by a temperature of 60° C. for 6 hours, but it is destroyed at 100° C. for 15 minutes.

The poisonous principle is filterable through porcelain, is not injured by drying, and can not be separated by precipitation with ammonium sulphate and subsequent dialysis.

The following chemical substances do not oxidize, neutralize, or precipitate the poisonous principle in horse serum: Butyric acid, permanganate of potash, citrate of soda, alcohol, succinic peroxide acid (alphozone), hydrogen dioxide, and ammonium sulphate. The presence of chloroform or trikresol (0.4 per cent) does not interfere with this poisonous action.

Serums eight years old are as toxic as those freshly separated.

Exposure to X-rays does not affect the poisonous action of horse serum.

It requires about 10 days after the first injection of horse serum for a guinea pig to show susceptibility to a second injection. A guinea pig remains susceptible a very long time, at least 160 days.

As small a quantity as $\frac{1}{1,000,000}$ c. c. of horse serum was sufficient in one instance to render a guinea pig susceptible. Quantities

varying from $\frac{1}{200}$ to $\frac{1}{1000}$ c. c. almost invariably render guinea pigs highly susceptible when given in the toxine-antitoxine mixture.

One-tenth c. c. of horse serum injected into the peritoneal cavity of a susceptible guinea pig is sufficient to cause death. The same quantity inoculated subcutaneously may cause serious symptoms.

There is some evidence to show that the sensitizing substance in horse serum is the same as the poisonous substance. The sensitizing substance is not affected by precipitation with ammonium sulphate and dialysis.

Guinea pigs may be sensitized with horse serum that has been dried and redissolved.

The sensitizing substance is not affected by a temperature of 60° C. for 6 hours.

It is probable that small quantities of horse serum render a guinea pig more susceptible than do large quantities. If this be true, it is due, perhaps, to the fact that large quantities, owing to slow absorption or prolonged reaction, partly immunize the guinea pig at the same time that it is being sensitized.

The sensitizing substance apparently is not free in the blood serum of guinea pigs.

An active immunity against this toxic principle may readily be established by repeated injections of horse serum, at short intervals, into a guinea pig. Although guinea pigs may be immunized actively in this manner we have not yet succeeded in transferring this immunity in the blood serum or body juices to another guinea pig. It therefore appears that the immune bodies, if such exist against the toxic action of horse serum, are not free in the blood and body juices contrary to the case in diphtheria.

Guinea pigs may be sensitized to the toxic action of horse serum by feeding them with horse serum or horse meat.

The fact that guinea pigs may be rendered susceptible by the feeding of strange proteid matter opens an interesting question as to whether sensitive guinea pigs may also be poisoned by feeding with the same serum given after a proper interval of time. If man can be sensitized in a similar way by the eating of certain proteid substances may not this throw light upon those interesting and obscure cases in which the eating of fish, sea food, and other articles of diet habitually cause sudden and sometimes serious symptoms?

The susceptibility to the toxic action of horse serum is transmitted hereditarily from the mother guinea pig to her young.

These results upon the hereditary transmission of the susceptibility to the poisonous action of horse serum in guinea pigs may throw light upon the well-known hereditary tendency to tuberculosis in children born of a tuberculous parent. There are certain analogies between the action of tuberculosis and horse serum. Both

may produce a hypersusceptibility and also a certain degree of immunity. Now that we have proved that this hypersusceptibility or anaphylactic action in the case of horse serum may be transmitted hereditarily in guinea pigs, may it not throw light upon the fact that tuberculosis "runs in families?"

Demonstrations of the hereditary transmission of acquired characters are comparatively rare in biology. While there are several recorded instances demonstrating that immunity to certain infectious diseases may be transmitted from a mother to her young, yet, as far as we know, this is the first recorded instance in which hypersensitiveness, or anaphylaxis, has been experimentally shown to be transmitted from a mother to her young.

Other albuminous substances, such as skimmed milk, peptone, hemoglobin, egg albumin, and vegetable proteids possess no poisonous action upon guinea pigs sensitized with horse serum. Whether guinea pigs are rendered susceptible to a subsequent injection with the same albuminous matter with which they have been sensitized will be reported in a later paper.

We believe that the substance which sensitizes the animal is identical with that which later poisons it. However, the substance must first cause a reaction in the organism resulting in a production of antibodies. We have found that small quantities of horse serum produce, after a definite period of incubation, a condition of anaphylaxis; multiple or repeated injections produce immunity. We therefore possess in horse serum a substance capable of causing both anaphylaxis and prophylaxis.

It may be that man can not be sensitized in the same way that we have shown to be the case with guinea pigs. Children have, in a number of instances, been injected with antidiphtheric horse serum at short and long intervals without, so far as we are aware, causing death. Certain serums, for example, the antitubercle serum of Maragliano and the antirheumatic serum of Menzer, are habitually used by giving injections at intervals of days or weeks. In all such cases of frequent and repeated injections the amount which has been injected and the interval between the injections must be taken into account in relation to our work. Von Pirquet and Schick have shown that a second injection of horse serum into children causes an "immediate" or an "accelerated" reaction. Both the immediate and the accelerated reaction in children are characterized by symptoms of "the serum disease."

We might conclude that children may not be sensitized to the toxic action of horse serum by eating horse meat, for horse meat is a favorite article of diet in certain European countries and there is nothing upon record to show that the injection of horse serum in those countries is fraught with more danger than where this diet is not used. It should,

however, be borne in mind that our work has shown that guinea pigs may be sensitized with exceedingly minute quantities of a strange proteid, and that repeated injections cause an immunity, and it does not seem impossible that the same action may be true of food.

Man reacts to the first injection of horse serum after a period of eight to thirteen days; guinea pigs show no reaction as a result of the first injection; both man and guinea pigs react to a second injection. The reactions in man and the guinea pig differ, however, both in severity and in kind. The relation, therefore, that our observations upon the guinea pig may have in their application to man must await further study.

The fact that other animals beside man and the guinea pig react to a second injection of horse serum would seem to indicate that we are dealing with one and the same action.

We believe that our results make it probable that man may be rendered sensitive to the injection of a strange proteid, as is the case with the guinea pig and other animals, and that this explanation must be considered as well as the *status lymphaticus*, which has heretofore been assigned as the cause of sudden death following the injection of horse serum.

[POST SCRIPTUM.—After the galley proof of this article had left our hands an article by R. Otto entitled “Das Theobald Smithsche Phänomen der Serum-Ueberempfindlichkeit,” reprinted from Leuthold-Gedenkschrift, band 1, first came to our notice. His paper deals with some of the problems we have studied and his results are in harmony with many of our conclusions.]

TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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M. J. ROSENAU, Director.

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- I.—MATERNAL TRANSMISSION OF IMMUNITY TO DIPHTHERIA TOXINE.
- II.—MATERNAL TRANSMISSION OF IMMUNITY TO DIPHTHERIA TOXINE AND HYPERSUSCEPTIBILITY TO HORSE SERUM IN THE SAME ANIMAL.

BY

JOHN F. ANDERSON.



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1906.

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United States Public Health and Marine-Hospital Service.

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I.

MATERNAL TRANSMISSION OF IMMUNITY TO DIPHTHERIA TOXINE.

By JOHN F. ANDERSON,

Passed Assistant Surgeon, Assistant Director Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service.

When the Hygienic Laboratory undertook the work of preparing a standard unit for the measurement of antidiphtheric serum, one of the first necessities was a constant and reliable supply of guinea pigs weighing from 250 to 280 grams. It was estimated that 500 females in the breeding pens would insure a sufficient number for this, as well as for the other work of the laboratory. It occurred to me that perhaps we might use as breeders the pigs that had been used for the testing of antitoxin or determining the strength of diphtheria toxine and had fully recovered. Before placing such pigs in the breeding pens I thought it would be well first to test the young of a number of such used and recovered pigs to see if they were resistant to the action of diphtheria toxine. For this purpose 21 pigs were placed aside and their young tested either by the giving of a MLD or L+ dose, control pigs being used in every case from the stock pigs whose mothers had previously had no treatment. All of the animals were under exactly the same conditions as regards food, temperature, air, light, etc., both before and after testing.

The determination of this question is of a threefold importance:

First. We know from work by Rosenau and Anderson^a that there is a hypersusceptibility to the injection of horse serum, normal or antitoxic, transmitted by a mother pig which has had a toxine-antitoxin mixture or serum alone to her young. It is, therefore, manifest that young pigs from such mothers should not be injected with serum for the purpose of determining the absence of bacterial contamination. In this test it is usual to inject several cubic centimeters of the serum

^a Rosenau, M. J., and John F. Anderson: A study of the cause of sudden death following the injection of horse serum. Hygienic Laboratory Bulletin No. 29, U. S. Public Health and Marine-Hospital Service. Washington, 1906. 95 p. 8°.

Manuscript submitted for publication June 26, 1906.

under examination, and in the work referred to 1 c. c. was sufficient to cause the death of pigs with a hypersusceptibility transmitted from the mother.

Second. If treated and recovered pigs are used as breeders and their young prove more resistant to diphtheria toxine, then when tests of serum are made on such resistant pigs we would evidently obtain misleading results.

Third. If these young pigs are of average susceptibility the recovered pigs could be used as breeders, resulting in quite a saving in animals bought for breeding purposes.

The use of such used animals as breeders was the custom in two antitoxin laboratories that I personally know of, and I suggested it as one explanation of irregularities they encountered in the testing of antitoxin. Both eliminated these used animals from their breeding pens with a decided decrease in the number of irregular results.

No pigs have been bought for use in the Hygienic Laboratory since May 31, 1905, the number raised being ample. We obtained pigs from three sources for breeding purposes, by far the larger number being presented to the laboratory by the Bureau of Animal Industry, none of which, I am sure, for many generations back had any taint of diphtheria toxine. As to the other two sources of supply I can not be so sure; but all of those received at the laboratory were under 300 grams in weight and consequently would not have been used for work with diphtheria toxine. Since May, 1905, we have used 3,439 pigs for the testing of diphtheria toxine or antitoxin. During this time a careful search of the records shows a very small number of pigs which died much earlier than was to be expected with the dose given, and some of these presented pneumonia at the autopsy. Only three have failed to die acutely when used on the L+ dose, thus showing very plainly that marked resistance to diphtheria toxine is unusual in the pigs bred at the Hygienic Laboratory.

Theobald Smith,^a in giving the results of tests of the young of three female pigs in which there was an immunity transmitted from the mother, says that this may be due to (1) the influence of any preliminary treatment, (2) the influence of the male, (3) the influence of selection in breeding. He considers his data sufficient to rule out the first, but states that the mother of his most resistant pigs (No. 2944) had previously been treated with a toxine-antitoxin mixture and about four or five months afterwards put into the breeding pens. I think, in view of my results, that this treatment fully accounts for the immunity of her young.

^a Smith, Theobald: Degrees of susceptibility to diphtheria toxin among guinea pigs; transmission from parents to offspring. *Journ. med. research*, vol. 13, n. s. vol. 8, Feb., 1905, p. 341-348.

In regard to his third question I think that the results obtained at the Hygienic Laboratory with the pigs raised here show that in our guinea pigs, at least, insusceptibility to diphtheria toxine is very rare. I am inclined to think that the influence of artificial selection in breeding is of slight importance if previous treatment of the breeders with the diphtheria toxine-antitoxin mixture can be excluded for several generations back. I can conceive that by the selection of breeders who have shown a special resistance to diphtheria toxine a very resistant race of pigs may be bred.

It is not improbable that dealers and breeders of guinea pigs may buy at times used guinea pigs from persons engaged in work with diphtheria antitoxin and thus introduce unknowingly into their stock toxine-resisting pigs.

The first experiments to immunize animals during pregnancy against pathogenic bacteria were positive.^a Chauveau found that the young of sheep so immunized were immune to anthrax, and like results were arrived at by Arloing, Cornevin, and Thomas in symptomatic anthrax.

Ehrlich was the first to study the problem methodically, and his results have been confirmed and stand. He used mice that had acquired a high degree of antitoxic immunity through systematic feeding of ricin, abrin, and robin. He showed that the male (sperm) element was incapable of transmitting the immunity.

Ehrlich used female animals that were immune before becoming pregnant. By using animals that were being immunized during pregnancy his results were interpreted as negative, inasmuch as positive results could not be referred to an active intra-uterine immunization of the fetus. In all of these cases his results were positive in that about four weeks after birth a definite immunity was demonstrable. About one and a half months after birth there still remained some undoubted immunity, but in the course of three months all traces had disappeared.

This short immunity in the progeny of mothers was considered as passive immunity and rested on the transmission of antibodies from the mother. Against inheritance in the strict sense there was the fact that there was absolutely none present in the grandchildren of immune mothers.

Ehrlich, therefore, concludes that neither sperm nor germ transmits the immunity and so no inheritance in the strict sense takes place.

Ehrlich, by his "mother exchange" experiment, showed that the antitoxins furnished in intra-uterine life did not long (21 days) remain in the young organism. He showed positively that the milk was the

^aThe above summary of a part of the literature upon the influence of heredity in immunity is largely taken from the article by Morgenroth in *Handbuch der pathogenen Mikroorganismen*, 4 bd., p. 784. Those interested will find this an excellent discussion of the subject with bibliography.

vehicle by which the suckling organism received its antitoxin and with the length of the suckling furnishes it with an increasing immunity. The long persistence of the immunity depended upon a transfer of antibodies through the milk. By the immunization of a nursing mother mouse (after birth of the litter) Ehrlich was able to transmit immunity to swine-plague to the nursing young.

Ehrlich and Hübener showed that Tizzoni and Centani had erred when they appeared to show that in rabbits the progeny of a male immune to hydrophobia and a female immune to tetanus was immune to hydrophobia. In experiments with tetanus-immune guinea pigs and mice they obtained results in entire harmony with the previous results of Ehrlich; and, opposed to Tizzoni's reports, established that in tetanus also no transmission occurs through a male, but that only through the mother does transmission of immunity take place which, by the end of the second and positively by the end of the third month, disappears.

Naillard came to the same conclusions from experiments on guinea pigs and rabbits.

The results of Wernicke on diphtheria-immune guinea pigs were also the same. "In diphtheria the immunity is not transmitted by the father, but the mother only." This immunity can not be detected in the grandchild, but remains longer in the first generation (the children), for in three months a considerable immunity is still present.

Transmission of immunity through the milk also occurs in guinea pigs.

Klemperer found in eggs of tetanus-immune hens tetanus antitoxin in the yolk, not in the white.

Kitt injected hens with eggs derived from chicken-cholera-immune hens and obtained immunity.

Sclavo immunized hens against diphtheria by injection of weakened cultures, and found that the whites of the eggs protected guinea pigs against lethal doses of diphtheria bacilli.

Tables Nos. 1 and 2 show the results of tests of the young of female guinea pigs that had recovered from the effects of an injection of toxine alone or of the toxine-antitoxin mixture. These animals were put aside for breeding after having been under observation 35 days after injection, which is the time all animals used for antitoxin work in the laboratory are kept under observation.

Table No. 1 shows the results of the tests of the young pigs against an L+ dose, and Table No. 2 against an MLD.

TABLE NO. 1.—*Showing resistance to the L+ dose in guinea pigs born of a mother treated with a single injection of toxine or toxine-antitoxin mixture.*

Mothers.							Young pigs.						Controls.	
No.	Treatment.				Result.		No.	Dose.		Result.			Result.	
	Toxine.		Serum.					Toxine.	Serum.	Death.	Recovery.			
	No.	Amount.	No.	Amount.	Reaction.	Paralysis.					Reaction.	Paralysis.	Death.	Recovery.
608	29 ^a	0.002	0	0	Ulcer.	—	608A	*0.22	1 <i>iu</i>	3-22	2-19
1424	9	.12	Ehr.	1 <i>iu</i>	—	—	1424A	.22	1 <i>iu</i>	8-3	5-7
							1424B	.22	1 <i>iu</i>	7-2	5-0
1992	9	.23	A4	1 <i>iu</i> +	—	—	1992A	.22	1 <i>iu</i>	—	—	2-6
1524	7	.21	B14	1 <i>iu</i> +	—	+	1524C	.22	1 <i>iu</i>	Ulcer.	—	2-1
1909	5	.133	140	$\frac{1}{400}$	—	—	1909A	.22	1 <i>iu</i>	2-15	2-15
1773	17A	.006	0	0	Ulcer.	—	1773A	.22	1 <i>iu</i>	2-17	3-7
1909	5	.133	140	$\frac{1}{400}$	—	—	1909B	.22	1 <i>iu</i>	3-16	2-22
608	29 ^a	.002	0	0	Ulcer.	—	608E	.22	1 <i>iu</i>	3-8	2-12
1907	5	.133	137	$\frac{1}{200}$	—	—	1907A	.22	1 <i>iu</i>	3-3	3-3
1946	15A	.3	B17	1 <i>iu</i>	—	—	1946C	.22	1 <i>iu</i>	Induration.	—	3-3
							1946A	.22	1 <i>iu</i>	Induration.	2-17
							1946B	.22	1 <i>iu</i>	Ulcer.	—	3-0
1766	17A	.005	0	0	Ulcer.	—	1766A	.22	1 <i>iu</i>	3-0	3-0
							1766B	.22	1 <i>iu</i>	2-19	3-0
1902	5	.133	181	$\frac{1}{600}$	—	—	1902A	.22	1 <i>iu</i>	Ulcer.	+	2-12
							1902B	.22	1 <i>iu</i>	Ulcer.	+	2-12
1905	5	.133	137	$\frac{1}{200}$	—	—	1905A	.22	1 <i>iu</i>	Ulcer.	+	3-0
2264	19	.007	0	0	Ulcer.	+	2264C	.22	1 <i>iu</i>	2-14	2-12
3827	7	.22	201	$\frac{1}{350}$	—	—	3827C	.22	1 <i>iu</i>	Ulcer.	—	3-2
608	29 ^a	.002	0	0	Ulcer.	—	608B	†.48	1 <i>iu</i>	2-23	2-3
1524	7	.21	B14	1 <i>iu</i> +	—	+	1524A	†.49	1 <i>iu</i>	Ulcer.	+	2-21
							1524B	.49	1 <i>iu</i>	7-5	2-21
1277	5	.130	IX-7	1 <i>cc</i>	—	—	1277B	†.50	1 <i>iu</i>	3-20	3-6

* No. 7.

† No. 15.

A study of this table shows that of 14 mothers, 7, or 50 per cent, transmitted an immunity to their young sufficient to withstand the effects of an L+ dose; all living except Nos. 1424A, 1424B, and 1524B, which lived 3, 2, and 4 days, respectively, longer than their controls. Of a total number of 24 young pigs shown in this table, 13, or 54.16 per cent, were resistant to an L+ dose.

Of the mothers that received the toxine-antitoxin mixture, 7, or 70 per cent, transmitted an immunity to their young.

The fact that no mother which received a dose of toxine alone transmitted an immunity to her young is very plainly shown.

TABLE NO. 2.—*Showing resistance to the MLD of guinea pigs born of a mother treated with a single injection of toxine or a toxine-antitoxin mixture.*

Mothers.							Young pigs.							Controls.	
No.	Treatment.				Result.		No.	Dose.		Result.			Result.		
	Toxine.		Serum.		Reaction.	Paralysis.		Toxine.	Serum.	Death.	Recovery.		Death.	Recovery.	
	No.	Amount.	No.	Amount.							Reaction.	Paralysis.			
608	29a	0.002	0	0	Ulcer.	—	608F	*0.005	0	2-5	2-18	
1278	5	.130	IX-17	$\frac{1}{100}$	—	—	1278C	*.005	0	Ulcer.	+	4-1	
1907	5	.133	137	$\frac{1}{260}$	—	—	1907B	*.005	0	Ulcer.	—	
1277	5	.130	IX-7	1 cc.	—	—	1277A	*.006	0	3-12	2-13	
1440	31B	.006	—	—	Indurated.	—	1440B	*.006	0	2-10	2-5	
1445	34A	.006	0	0	Ulcer.	—	1445A	*.006	0	2-8	2-21	
608	29a	.002	0	0	Ulcer.	—	608D	†.01	0	4-0	3-7	
1278	5	.130	IX-17	$\frac{1}{100}$	—	—	1278A	†.01	0	Ulcer.	+	3-19	
1440	31B	.006	—	—	Indurated.	—	1446A	†.01	0	2-21	5-3	
1773	17A	.006	—	—	Ulcer.	—	1773B	†.01	0	4-23	4-9	
1445	34A	.006	0	0	Ulcer.	—	1445B	†.02	0	2-7	2-5	
1277	5	.130	IX-17	1 cc.	—	—	1277C	†.02	0	2-12	2-12	
1278	5	.130	IX-17	$\frac{1}{100}$	—	—	1278B	†.02	0	Ulcer.	+	2-12	
1426	9	.16	Ehr.	1 <i>iu</i>	—	—	1426A	†.006	0	4-0	3-3	
1427	9	.18	Ehr.	1 <i>iu</i>	—	—	1427B	†.006	0	Ulcer.	—	2-17	
1497	5	.130	B14	1 <i>iu</i> +	—	+	1497A	†.006	0	Ulcer.	—	2-22	
							1497B	†.006	0	Ulcer.	—	3-8	
1905	5	.133	137	$\frac{1}{260}$	—	—	1905B	†.006	0	Ulcer.	+	3-6	
							1905C	†.006	0	Ulcer.	+	3-6	
4495	7	.19	B27	1 <i>iu</i>	+	+	4495A	†.007	0	—	2-2	
							4495C	†.007	0	—	1-12	

* No. 9.

† No. 15.

‡ No. 7.

An examination of this table shows that of 12 mothers 6, or 50 per cent, transmitted an immunity to their young.

Of a total number of 21 young pigs treated 11, or 52 per cent, were resistant to a fatal dose for control pigs.

Of the mothers that received the toxine-antitoxin mixture 75 per cent transmitted an immunity to their young.

No mother that had received an injection of toxine alone transmitted this immunity.

It will be noticed in both tables that where an immunity is transmitted to the young all of the litter are immune to about the same degree.

The question will naturally be asked, Why is this immunity not transmitted by all of the mothers treated with the toxine-antitoxin mixture? I can not answer this question positively, but suggest that it may be due to the fact that some of the pigs produce more antitoxin than others. It is a well-known fact among producers of diphtheria antitoxin that some horses can never be made to produce a serum of even 250 units, which is considered a rather low potency serum. Such may be the case with guinea pigs.

The following data, kindly furnished me by Dr. J. J. Kinyoun, director of the biologic laboratories of H. K. Mulford & Co., is of interest in this connection. It will be seen by reference to the table (No. 3) that some horses, in spite of prolonged treatment, never produce any antitoxin.

TABLE NO. 3.—*Table showing that some horses, in spite of prolonged treatment, fail to produce any antitoxin, or only small amounts.*

No.	Duration of treatment.	Number MLD for 250 gm. G. P.	Num- ber of trials.	Highest value. <i>Units.</i>	Result.
1	14 weeks.....	1,280,000	4	0	Died.
2	18 weeks.....	1,110,000	5	50	Do.
3	19 weeks.....	1,010,000	4	100	Do.
4	20 weeks.....	2,080,000	5	100	Do.
5do	1,800,000	3	100	Do.
6	22 weeks.....	1,520,000	5	0	Returned.
7do	2,390,000	10	100	Do.
8	24 weeks.....	1,980,000	6	0	Died.
9	25 weeks.....	2,810,000	12	100	Do.
10do	2,590,000	5	0	Transferred.
11do	3,990,000	8	0	Do.
12	26 weeks.....	5,710,000	12	100	Died.
13	28 weeks.....	3,520,000	10	100	Returned.
14	30 weeks.....	3,770,000	6	100	Died.
15	32 weeks.....	4,600,000	12	0	Transferred.
16	36 weeks.....	5,530,000	11	50	Died.
17do	4,000,000	15	100	Do.
18	37 weeks.....	4,500,000	14	100	Returned.
19	39 weeks.....	6,030,000	9	100	Died.
20	47 weeks.....	19,500,000	23	150	Transferred.
21	48 weeks.....	10,560,000	20	150	Do.
22do	9,090,000	17	100	Returned.

Attention is called especially to horses Nos. 1, 6, 8, 10, 11, and 15, which never produced serum with antitoxic properties.

THE EFFECT OF REPEATED INJECTIONS IN THE MOTHER ON HER YOUNG.

At the suggestion of Doctor Rosenau a number of female guinea pigs were given repeated injections either of antitoxin alone or of one unit of antitoxin plus slightly more than the L^0 dose of toxine in order to study the effects of repeated injections in the mother on her young. An untreated male was placed in the pen with them. The young were allowed to remain with their mother until the day before being tested. They were tested in most cases against an $L+$ dose, though in some cases a larger dose, either one and a third or one and a fourth times the $L+$ dose, was given.

Pigs Nos. 4E, 4F, 8G, and 8H received eight and one-third times the MLD.

GUINEA PIG NO. 4.

May 25, 1905. Given 0.15 c. c. toxin No. 7 ($L+ .21$) + 1 immunity unit Ehrlich 15. IV .05.

May 29. Same treatment.

June 9. 0.18 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. IV .05.

June 16. 0.19 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. IV .05.

June 26. 0.19 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. IV .05.

July 12. 0.19 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. IV .05.

Litter No. 1.

July 28, 1905. 4A and 4B born.

August 25. 4A given 0.22 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. VIII .05. Moderate reaction at site on third day. Recovered. Control died in 3 days and 3 hours.

August 25. 4B given 0.22 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. VIII .05. Died in 6 days and 3 hours. Control died in 3 days and 3 hours.

Litter No. 2.

November 7, 1905. 4C and 4D born.

January 6, 1906. 4C given 0.22 c. c. toxine No. 7 + 1 immunity unit B27. No reaction. Control died in 3 days and 7 hours.

January 24. 4D given 0.293 c. c. toxine No. 7 ($=1\frac{1}{3}$ times the $L+$ dose). Induration followed by small ulcer. Recovered. Control died in 1 day and 15 hours.

Litter No. 3.

May 21, 1906. 4E and 4F born.

June 22. Both given 0.05 c. c. toxine No. 7 (MLD=0.006 c. c.). Slight induration third day. Controls died in 1 day and 4 hours and 22 hours, respectively

GUINEA PIG NO. 5.

Same treatment as No. 4.

Litter No. 1.

July 27, 1905. 5A and 5B born.

September 9. Both given 0.22 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. IX .05. Slight induration at site in both pigs. Recovered. Controls died in 3 days and 12 hours.

Litter No. 2.

October 27, 1905. 5C and 5D born.

January 6, 1906. Both given 0.22 c. c. toxine No. 7 + 1 immunity unit B27. No reaction in either pig. Controls died in 3 days and 7 hours.

Litter No. 3.

February 3, 1906. 5E born.

March 17. Given 0.293 c. c. toxine No. 7 ($1\frac{1}{2}$ times the L + dose) + 1 immunity unit B28. Very slight reaction fourth day. Recovered. Control died in 1 day and 18 hours.

Litter No. 4.

April 12, 1906. 5F and 5G born.

June 5. Both given 0.275 c. c. toxine No. 7 ($1\frac{1}{4}$ times the L + dose) + 1 immunity unit Ehrlich 15. VI .06. Both showed induration followed by ulcer at site. Control died in 1 day and 21 hours.

GUINEA PIG NO. 6.

Same treatment as No. 4.

Litter No. 1.

September 7, 1905. 6A and 6B born.

October 20. Both given 0.22 c. c. toxine No. 7 + 1 immunity unit B25. No reaction. Controls died in 3 days and 2 hours.

Litter No. 2.

November 8, 1905. 6C, 6D, 6E, and 6F born; 6C, 6E, and 6F used for other work.

January 24, 1906. 6D given 0.293 c. c. toxine No. 7 ($1\frac{1}{2}$ times the L + dose) + 1 immunity unit B27. Small ulcer. Recovered. Control died in 1 day and 20 hours.

Litter No. 3.

February 17, 1906. 6G born.

March 17. Given 0.293 c. c. toxine No. 7 ($1\frac{1}{2}$ times the L + dose). Very slight reaction. Control died in 1 day and 18 hours.

Litter No. 4.

April 26, 1906. 6H and 6I born.

June 5. Both given 0.275 c. c. toxine No. 7 ($1\frac{1}{4}$ times the L + dose). No reaction in either pig. Control died in 1 day and 21 hours.

GUINEA PIG NO. 7.

May 25, 1905. Given 250 units antitoxin.

June 9. Given 600 units antitoxin.

June 16. Given 900 units antitoxin.

June 26. Given 1,000 units antitoxin.

July 12. Given 1,500 units antitoxin.

Litter No. 1.

July 26, 1905. 7A born.

August 16. Given 0.22 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. VIII .05. Small ulcer. Recovered. Control died in 3 days and 7 hours.

August 24. The mother pig was killed, blood drawn, allowed to clot, and serum tested to 12, 25, and 50 units. All the pigs died in about 24 hours, showing that her serum contained considerably less than 12 units per cubic centimeter.

GUINEA PIG NO. 8.

Same treatment as No. 7.

Litter No. 1.

July 29, 1905. 8A, 8B, and 8C born. 8B and 8C died.

September 15. 8A given 0.22 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. VIII .05. Died in 7 days and 7 hours. Control died in 4 days.

Litter No. 2.

March 15, 1906. 8D, 8E, and 8F born.

April 27. 8D given 0.22 c. c. toxine No. 7 + 1 immunity unit Ehrlich 15. VIII .06. No reaction. Control died in 4 days and 8 hours.

April 27. 8E and 8F given same injection as 8D. Both died on the third day. Controls died on the third day.

Litter No. 3.

May 20, 1906. 8G, 8H, and 8I born.

June 22. 8G and 8H given 0.05 toxine No. 7 (MLD = 0.006 c. c.). 8G died in 1 day and 4 hours. Control died in 22 hours. 8H showed slight induration on third day. Recovered. Control died in 1 day and 4 hours.

A study of the above results shows that the young of all the mothers that were treated by repeated injections of the toxine-antitoxin mixture had a marked resistance to an L+ dose; all survived except one, 4B, which died, but lived 3 days longer than the control. Four (4D, 5E, 6D, and 6G) withstood one and a third times the L+ dose; this dose uniformly caused the death of the controls in less than 2 days. Four (5F, 5G, 6H, and 6I) resisted one and a fourth times the L+ dose.

Of four pigs tested against eight and a third times the MLD three recovered (4E, 4F, and 8H); one (8G) showed the average susceptibility to the toxine.

The members of the fourth litter are as resistant as those of the first. The immunity seems to be greater in those pigs born of mothers treated with the toxine-antitoxin mixture than in those treated with the antitoxin alone. Pigs Nos. 4, 5, and 6 received a total of only 6 units, given in doses of 1 unit plus an amount of toxine slightly greater than the L⁰ dose, while pigs 7 and 8 received 4,250 units. Of seven young of these last two mothers, three recovered, one lived 3 days longer than the control, and three showed no resistance.

Moreover, it would seem that the immunity produced by the injection of large amounts of antitoxin alone is not as lasting as that produced by small amounts plus small doses of toxine.

IMMUNITY NOT TRANSMITTED TO SECOND GENERATION.

Two female guinea pigs born of mother No. 6 (see p. 15), and from a litter of which the other members had shown marked resistance to diphtheria toxine, were placed with a male pig born of untreated parents. Each female had two young. These were given an L+ dose

to determine whether the immunity was transmitted to the second generation (grandchildren). The results are given below:

Guinea pig No. 6ac. Given 0.22 c. c. toxine No. 7+1 immunity unit Ehrlich 15.VI .06. Died in 3 days 14 hours. Control died in 3 days 17 hours.

Guinea pig No. 6bc. Given 0.22 c. c. toxine No. 7+1 immunity unit Ehrlich 15.VI .06. Died in 3 days 20 hours. Control died in 3 days 14 hours.

Guinea pig No. 6ae. Given 0.22 c. c. toxine No. 7+1 immunity unit Ehrlich 15.VI .06. Died in 4 days 4 hours. Control died in 3 days 17 hours.

Guinea pig No. 6be. Given 0.22 c. c. toxine No. 7+1 immunity unit Ehrlich 15.VI .06. Died in 3 days 17 hours. Control died in 3 days 14 hours.

From the above it seems plain that the resistance to diphtheria toxine is not transmitted to the second generation.

THE CUMULATIVE EFFECT OF DIPHTHERIA TOXINE.

An attempt was made to immunize female guinea pigs by repeated small injections of diphtheria toxine. Doses considerably less than the MLD and not sufficient to cause a perceptible reaction were given at intervals of about 7 days. Before an amount equal to an MLD had been given the animal in each case died. These results are in exact accord with the work of Behring and Kitashima,^a who found that guinea pigs, when given daily injections of diphtheria toxine and when the total amount injected was only $\frac{1}{400}$ of an MLD, after a time died with the post-mortem lesions of poisoning from diphtheria toxine. Instead of being able to produce an immunity to the toxine a hypersusceptibility was produced.

A study of Tables 1 and 2 will show that in no case in which the preliminary treatment of the mother was of toxine alone was there an immunity transmitted by the mother to her young. This at first seemed to me a remarkable fact. I conceive the reason of the failure for this immunity to be transmitted by pigs whose preliminary treatment was toxine alone to be due to the fact that the mother pig was not immunized by a single dose of toxine, and that it is difficult to produce an active immunity in guinea pigs by the repeated injections of toxine, for before this result is obtained the cumulative effect of the toxine kills the animal.

It seems to me that instead of calling it a hypersusceptibility to the poison, as did Behring and Kitashima, it would be more proper to consider this action due to the cumulative effect of repeated small doses of the toxine.

It is well known among clinicians that one attack of diphtheria, rheumatism, or pneumonia predisposes to a subsequent one. This may more properly be considered due to an induced hypersusceptibility, whereas the repeated injections of toxine, as in the case of the guinea pigs, is a cumulative action.

^a Von Behring and Kitashima: Über Verminderung und Steigerung der ererbten Gift empfindlichkeit. Berl. klin. Woch., 1901, p. 157.

II.

MATERNAL TRANSMISSION OF IMMUNITY TO DIPHTHERIA TOXINE AND HYPERSUSCEPTIBILITY TO HORSE SERUM IN THE SAME ANIMAL.

We know (loc. cit., p. 14) that the young of female guinea pigs that have received either before or during pregnancy toxine-antitoxin mixtures are hypersusceptible to an injection of horse serum either normal or antitoxic. It therefore occurred to me that it would be very interesting to determine whether such young pigs were also immune to diphtheria toxine.

For this purpose it was necessary first to test the immunity against the MLD, and if the animal recovered to test its hypersusceptibility to horse serum. We know (loc. cit., p. 17) that treatment with toxine alone does not render a guinea pig susceptible to a subsequent injection of horse serum.

Guinea pigs born of a susceptible mother and from a litter of which the other members were immune to diphtheria toxine were also used to test the transmission of hypersusceptibility to horse serum. The results are as follows:

FAMILY NO. 1.

Mother guinea pig No. 4495. 103 days before the birth of young given 0.19 c. c. toxine No. 7 + 1 immunity unit B27. Local reaction, paralysis; recovered.

April 25, 1906. Nos. 4495A, 4495B, and 4495C born.

June 22. Nos. 4495A and 4495C given 0.007 c. c. toxine No. 7. No reaction third day. Controls died in 2 days 2 hours and 1 day 12 hours.

The results of this test showed a distinct immunity to diphtheria toxine.

June 26. Both of the above and 4495B, which had received no toxine, were given 2 c. c. normal horse serum. All three died in less than 45 minutes.

FAMILY NO. 2.

Mother guinea pig No. 4. (For treatment of mother see p. 14.)

June 22, 1906. Guinea pigs Nos. 4E, 4F, received $8\frac{1}{3}$ times the MLD (see p. 14).

Both showed slight induration on the third day; recovered.

June 26. Guinea pigs Nos. 4E, 4F, and 4G were given 2 c. c. normal horse serum.

All three died in less than 45 minutes.

FAMILY NO. 3.

Mother guinea pig No. 8. (For treatment of mother see p. 16.)

June 22, 1906. Guinea pig No. 8G given $8\frac{1}{2}$ times the MLD. Showed slight induration on the third day; recovered.

June 26. Guinea pigs Nos. 8G and 8I given 2 c. c. normal horse serum. Both died in less than 45 minutes.

Four control pigs of about the same age and weight, born of untreated mothers, received 4 c. c.—twice the amount given the test pigs—of normal horse serum. None showed any inconvenience as a result of the injection.

It will be readily seen from the above that a mother can transmit to the same young two properties, viz, immunity to diphtheria toxine and hypersusceptibility to horse serum.

It is therefore very manifest that female guinea pigs that have received the toxine-antitoxin mixtures should not be used as breeders by those engaged in work with diphtheria antitoxin. On account of the transmitted immunity misleading results in the testing of antitoxin and toxine will be had. On account of the hypersusceptibility to the injection of horse serum pigs derived from such a source, when used to determine the presence of bacterial or toxic impurities may die, not from the presence of such impurities, but on account of a hypersusceptibility to horse serum transmitted from the mother.

TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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VARIATIONS IN THE PEROXIDASE ACTIVITY OF THE
BLOOD IN HEALTH AND DISEASE.

BY

JOSEPH H. KASTLE

AND

HAROLD L. AMOSS.



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VARIATIONS IN THE PEROXIDASE ACTIVITY OF THE BLOOD IN HEALTH AND DISEASE.^a

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It is to Schönbein^b that we are indebted for the observation that aqueous extracts of various plant and animal tissues have the power of actively decomposing hydrogen peroxide and of greatly accelerating oxidations by means of this substance. It was shown, for example, that when a freshly prepared extract of malt is added to water containing small amounts of hydrogen peroxide and tincture of guaiacum the solution becomes dark blue in color, owing to the oxidation of the guaiacum. So delicate is this reaction that for many years it afforded the most sensitive test for hydrogen peroxide known to chemists. It was also observed by Schönbein^c, during the progress of these investigations, that blood corpuscles and ferrous salts have the power of rendering active the oxygen of hydrogen peroxide toward such oxidizable substances as guaiacum, indigo, and a mixture of potassium iodide and starch; and Hiss^d pointed out that the activity of blood corpuscles in this regard diminishes in proportion to the withdrawal of iron therefrom. Schönbein, therefore, reached the conclusion that blood corpuscles owe their power to render active the oxygen of hydrogen peroxide to the iron which they contain, and in this connection he cited the interesting observation that blood corpuscles do not

^a Manuscript submitted July 5, 1906.

^b Bericht über die Verhandlungen der Naturforschenden Gesellschaft in Basel, III, 697-721.

^c Ibid. II, 9-15 (see also Jour. f. Prakt. Chem., Vol. 75, p. 73).

^d Private communication to Schönbein.

lose their power of rendering oxygen active, either through heating to boiling, or as the result of partial putrefaction. This would seem to indicate, as pointed out by Schönbein, that their power to render active the oxygen of hydrogen peroxide depends less on their organization as living cells than on their iron content.

Schönbein^a made the further interesting observations that dried blood corpuscles are more active than fresh in the production of guaiacum blue from a mixture of guaiacum and hydrogen peroxide, and that hydrocyanic acid retards these oxidations in much the same way that it hinders alcoholic fermentation and the sprouting of seeds. He arrived at the conclusion; therefore, that hydrocyanic acid kills animals so rapidly for the reason that it hinders catalysis and interferes with respiration.

Aside from their general interest the chief importance attaching to these earlier observations of Schönbein is that these reactions afforded delicate tests both for hydrogen peroxide and blood; and of the various tests for blood^b that have been proposed from time to time, certainly the greater number, if not all, depend on the production of some colored substance, as the result of the oxidation of a chromogenic substance by hydrogen peroxide and blood.

During recent years, however, the oxidizing ferments of the blood have been the subject of further investigations. Lumière and Chevrotier,^c for example, have prepared a protoplasmic extract of red corpuscles by vigorously centrifugalizing a mixture of blood and isotonic liquid, collecting the corpuscles, and washing several times with the isotonic liquid. The washed corpuscles were then subjected to alternate freezing and thawing in order to disintegrate them, and the mixture centrifugalized. The liquid was then filtered and rendered isotonic by means of sodium chloride. It was again filtered and preserved in sterilized flasks. This liquid, which the authors have called hæmoplase, rapidly loses oxygen in vacuum, becoming violet black in color, the red color being restored by agitation with air. It was found by these observers to possess the properties of an oxidase to a very marked degree.

Quite recently, Jolles and Oppenheim^d have made a quantitative study of the power of the blood of man and certain of the lower animals to decompose hydrogen peroxide. It has been found as the result of these investigations, that the blood of amphibious animals decomposes hydrogen peroxide very slowly as compared with the rate of

^a Bericht über die Verhandlungen der Naturforschenden Gesellschaft in Basel, IV, 410 and 767.

^b Schaer, Zeit. f. anal. Chem., 1903, p. 1; and Archiv der Pharmacie, 238 (1900), 42-48.

^c Compt. rend., 141 (1905), 142-143.

^d Zeit. f. anal. Chem., 44 (1904), 1-5; and Münch. Med. Woch., 51, 2083-2085; and also Virchow's Archiv (1905), 180, 185 and 225.

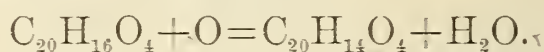
decomposition brought about by the blood of man and the higher animals, and that the blood of fishes possesses the least catalytic activity of any blood thus far examined. It has also been observed that the power of the blood of man to decompose hydrogen peroxide suffers a marked diminution in certain pathological conditions such as tuberculosis, nephritis, and cancer. They have found further that the catalase of blood is destroyed by boiling, and also by acids; that it is present exclusively in the formed elements of the blood, and that roughly, at least, it is proportional to the amount of hemoglobin.

Sometime ago, it was observed by one of us (Kastle) that the yellowish filtrate from boiled blood has the power of effecting the oxidation of phenolphthalin in alkaline solution, whereas, solutions of blood salts, with and without iron, prepared according to the analyses given in Bunge's *Physiologic and Pathologic Chemistry* (pp. 212-213), do not possess this property. Up to the present, we have not had an opportunity to investigate this interesting difference in conduct of these two solutions. It led to the notion, however, that it would probably be of interest to determine the oxygen-carrying power of the blood in alkaline solution under various conditions of health and disease, using phenolphthalin as the oxidizable substance and hydrogen peroxide as the oxidizing agent. In other words, the attempt has been made to determine what may be called the peroxidase activity of the blood of man under various conditions of health and disease.

THE BLOOD AS AN OXYGEN-CARRIER IN THE OXIDATION OF PHENOL-PHTHALIN BY HYDROGEN PEROXIDE.

THE REACTION AND MODE OF PROCEDURE.

Phenolphthalin or dioxytriphenylmethane carbonic acid is the leuco compound of phenolphthalein. On oxidation, it passes into phenolphthalein in the sense of this equation:



Hence, if the oxidation takes place in alkaline solution, we have the production of a deep purplish red compound (phenolphthalein in alkali) from a colorless salt. The oxidation of phenolphthalin may be accomplished by various peroxides, such as lead and manganese peroxide, benzoyl peroxide, etc., and by the plant oxidases. In fact, Kastle and Shedd^a several years ago proposed a neutral solution of this compound as a reagent for the plant oxidases. Phenolphthalin is also slowly oxidized by hydrogen peroxide in neutral and alkaline solution. As is the case with many of the oxidations of this character, however, the change is greatly accelerated by various oxygen-carriers, such as platinum black, etc., and as indicated in the foregoing, by the peroxidase of blood. It will be seen from our results, which are given in the following pages, that when allowed to stand alone an alkaline solution of phenolphthalin and hydrogen peroxide gives only a faint pink coloration. If, however, a very small quantity of blood be added to such a solution it soon acquires the deep, purplish red coloration, characteristic of phenolphthalein in alkali, indicating that under the influence of blood or an oxygen-carrier, hydrogen peroxide is able to effect the oxidation of phenolphthalin with far greater rapidity than when allowed to react alone.

That a certain amount of free alkali is essential to this change may be gathered from the following: Six solutions were prepared, each containing 2 c. c. of fresh blood solution (Porch, normal), 1 cu. mm. to 250 c. c. and 5 c. c. of a reagent, containing 0.032 gram phenolphthalin, 0.0034 gram hydrogen peroxide, and 1 c. c. N 10 sodium hydroxide, the whole diluted to 100 c. c. To three of the mixed solutions 1 c. c. of water was added. These three solutions were labeled A. To each of the remaining solutions 1 c. c. of N 10 sodium hydroxide was added. These solutions containing the excess of sodium hydroxide were

^aAmer. Chem. Jour., 26 (1901), 526-539.

labeled B. One set of the solutions A and B was then allowed to stand for fifteen minutes at room temperature, $30^{\circ}\text{C}.$, at the end of which interval 1 c. c. of N 10 sodium hydroxide was added to A and 1 c. c. of water was added to B. The depth of color of each was then determined by comparison with standard phenolphthalein placed at five divisions on the colorimeter scale, immediately and fifteen minutes after the final addition of sodium hydroxide and water with the following results:

15-minute series.

READINGS ON COLORIMETER.

Time.	A.	B.
Immediately.....	^a 175.	5
15 minutes	10.8	^b 4.6

^a It should be borne in mind that a large number on the scale of the colorimeter (Duboscq-Pellin) signifies a faint coloration and the presence of a small amount of the colored substance, whereas, conversely, a small number on the colorimeter scale indicates a greater depth of color and a correspondingly larger amount of colored substance. For further details regarding this method of making the color comparisons see footnote ^b, p. 15, of this communication.

^b B of course had stood altogether 30 minutes in contact with 1 c. c. N/10 sodium hydroxide, at a total dilution of 8 to 9 c. c.

A second pair of solutions A and B was allowed to stand in glass-stoppered bottles at $30^{\circ}\text{C}.$ for two hours, at the end of this time 1 c. c. of N 10 sodium hydroxide was added to A and 1 c. c. of water to B. The depth of color of each was then determined by comparison with a standard solution of phenolphthalein solution in alkali in the colorimeter, the standard tube of the colorimeter being placed at 5 divisions on the scale, immediately and after standing fifteen minutes, with the following results:

Two-hour series.

READINGS ON COLORIMETER.

Time.	A.	B.
Immediately.....	178	6.7
15 minutes	3.9	6.7

The third set of solutions was allowed to stand for three hours at ordinary temperature, at the end of which time 1 c. c. of N 10 sodium hydroxide was added to A and 1 c. c. of water to B. The color intensity of both solutions was then determined immediately in the manner already described with the following results:

Three-hour series.

READINGS ON COLORIMETER.

Time.	A.	B.
Immediately.....	235	7.6
15 minutes	65	7.5

It is evident from these results that the oxidation of phenolphthalin by blood and hydrogen peroxide takes place only in alkaline solution, and a comparison of the 15-minute, two, and three hour series with one another goes to show that on standing in contact with hydrogen peroxide and the sodium salt of phenolphthalin at the concentration indicated above, the blood loses a great deal of its oxygen-carrying power at the same time that it probably effects the decomposition of the hydrogen peroxide catalytically. (See the work of Jolles and Oppenheimer.) With the view of throwing still further light on these points, 2 c. c. of blood solution (1 cu. mm. blood to 250 c. c.) were added to solution A of the three-hour series and to solution B of the same series 2 c. c. of distilled water. These solutions were then allowed to stand at ordinary temperature and at the end of fifteen minutes and one hour the depth of color of each determined in the colorimeter in the manner already described with the following results:

READINGS ON COLORIMETER.

Time.	A.	B.
15 minutes	12.7	8.6
1 hour.....	6	9

Comparing the numbers under A with those given under A in the three-hour series, we note a remarkable increase in the depth of color and hence an increase in the amount of phenolphthalin oxidized, as the result of adding the second 2 c. c. of blood solution, thereby showing that while all other substances needful to effect the oxidation of the phenolphthalin were at hand in solution A of the three-hour series the oxygen carriers of the first portion of blood solution had been so altered by standing in contact with hydrogen peroxide and the sodium salt of phenolphthalin as to become largely incapable of effecting the oxidation.

It has also been observed that within certain limits the oxidation of phenolphthalin by blood and hydrogen peroxide is nearly proportional to the concentration of the sodium hydroxide. That such is the fact may be seen from the following: Two solutions were prepared and labeled (1) and (2). (1) contained 0.032 gram phenolphthalin, 0.0034 gram hydrogen peroxide, 30 c. c. N 100 sodium hydroxide, the whole made up to 100 c. c. with distilled water. (2) was the same as (1) except that it contained 21 c. c. N 10 sodium hydroxide. Bearing in mind that 10 c. c. N 100 or 1 c. c. N 10 sodium hydroxide are required respectively to neutralize the phenolphthalin present in these two solutions, it will be seen that the free alkali in (1) and (2) corresponds to 20 c. c. N 100 and 20 c. c. N 10 sodium hydroxide respectively. In order to determine the effect of alkali at these two concentrations on

the oxidizing power of blood, 5 c. c. of solutions (1) and (2) were taken and 2 c. c. of a normal blood solution, 1 cu. mm. to 250 c. c., added to each. The mixtures were then allowed to stand for the several intervals indicated below at the end of each of which the depth of color of each solution was determined by comparison with a standard solution of phenolphthalein in alkali by means of the colorimeter, the standard being set at 5 divisions on the colorimetric scale:

READINGS ON COLORIMETER.

Time.	(1)	(2)
1 hour.....	17.1	1.9
24 hours.....	17.25	5.6
48 hours.....	18	4.1

It is evident, therefore, that the amounts of phenolphthalin oxidized under these conditions are, for a short interval of time, nearly proportional to the concentration of the sodium hydroxide.

It should also be borne in mind that in alkaline solution, blood alone has the power of effecting the oxidation of phenolphthalin, and that this oxidizing power is not completely destroyed by boiling, although it is considerably weakened. Were this direct oxidizing power of the blood completely destroyed by heat, we should be inclined to refer its oxidizing power to the presence of an oxidase. If the oxidizing substance is really an oxidase, we must look upon it as possessing far greater stability than the plant and animal oxidases generally. Whether the oxidation of phenolphthalin by blood in alkaline solution in the presence or absence of hydrogen peroxide is referable to the same cause will be the subject of further investigation. It is sufficient for present purposes to bear in mind that at the dilution of blood employed in making these measurements of peroxidase activity—viz, 1 cu. mm. of blood to 250 c. c.—the direct oxidizing power of the blood in alkaline solution is extremely feeble, whereas, in the presence of hydrogen peroxide the oxidation of the phenolphthalin proceeds with considerable velocity.

MODE OF PROCEDURE.

It was found, as the result of a few preliminary observations, that in determining the peroxidase activity of the blood by this method, the greatest care would have to be exercised in order to obtain reliable and comparable results. Such being the case, the following mode of procedure was agreed upon: In the first place, the work was so arranged that the collection of samples of blood, together with the determination of the amount of hemoglobin in the several samples, was left to Amoss, whereas the chemical measurements and also the

preparation of the reagents required devolved upon the other party concerned in this investigation. By this arrangement it was hoped to secure greater accuracy than could otherwise be obtained.

In collecting the samples of blood, the following mode of procedure was agreed upon and rigorously adhered to. In nearly all cases the samples of blood were obtained from the lobe of the ear. When this was impracticable, from the tip of the fore finger. The part was gently stroked for some time in order to flush it with blood. A deep stab was then made with a blood lancet and two samples collected, one for the hemoglobin determination, using a Dare hemoglobinometer; the second was carefully collected in a 1 cu. mm. blood pipette, which was then carefully washed out with a small amount of distilled water, and the sample made up to 5 c. c. with distilled water. The determination of the peroxidase activity of the second sample was then made as soon as possible; never after a longer interval than three hours, except in those cases where it was desired to determine the effect of standing in contact with water on the peroxidase activity. The peroxidase activity of the several samples of blood was determined in the following manner:

The solution of blood in 5 c. c. of water was carefully poured into a 250 c. c. measuring flask, the bottle washed, and the solution exactly made up to 250 c. c. with distilled water. 2 c. c. portions of this more dilute solution were then accurately measured out, using a form of pipette described by Rosenau^a in his work on the determination of the immunity unit for standardizing diphtheria antitoxin and which, for such work as this now under consideration, possesses many advantages in point of accuracy over the older method of using the pipette. These 2 c. c. portions of the blood solution (1 cu. mm. blood to 250 c. c.) were then mixed with 5 c. c. of a reagent containing the following substances: 0.032 grams phenolphthalin, 21 c. c. N/10 sodium hydroxide, 10 c. c. hydrogen peroxide, containing .034 grams H_2O_2 in 100 c. c., the whole made up to 100 c. c. with distilled water. The mixtures of blood solution and the reagent were then preserved in glass-stoppered bottles for the desired intervals, usually one to twenty-four hours. During this time the solutions acquired the purplish red color of phenolphthalein in alkali, and at the end of the given interval the amount of phenolphthalein produced as the result of the oxidation of the phenolphthalin was determined by comparing the color of the solution with that of a standard solution of phenolphthalein in alkali containing 0.000318 grams of phenolphthalein, and 1 c. c. N/10 sodium hydroxide at a total dilution of 7 c. c. The color comparisons were made in a Duboscq-Pellin colorimeter, the readings being made in diffused light.

^a Bulletin 21, Hygienic Laboratory, April, 1905, fig. 13, p. 64.

That the amount of phenolphthalein formed as the result of the oxidation of phenophthalin can be accurately determined by this colorimetric method, provided an excess of alkali, not too great, is present in the solution, may be seen from the following observation:

A solution of phenolphthalein was prepared containing 0.159 grams of the substance in 100 c. c. of absolute alcohol. One cubic centimeter of this solution, which we will call solution A, was mixed with 5 c. c. of water and 1 c. c. N/10 sodium hydroxide. The color of this solution was then compared in the colorimeter with that of a standard solution of phenolphthalein containing 0.0318 grams of the compound in 100 c. c. of absolute alcohol, using the same quantity of water and sodium hydroxide. These solutions gave the following readings on the colorimeter:

Solution A.	Standard.
1.1	5
1	5

The theory for these solutions is 1:5, inasmuch as the stronger solution contains five times as much phenolphthalein as the standard.

On account of the very slight solubility of phenolphthalein in water, considerable difficulty has been encountered in the preparation of the standard solution of phenolphthalein with which to make the color comparisons. Hence it is, that during the progress of the investigation, several such standard solutions of phenolphthalein have been employed, so that, in the majority of cases, at least, the results obtained in the several series of experiments are not strictly comparable, one series with another, but only the results of any particular series among themselves.

Another reason why the results of any particular series of experiments are only comparable among themselves and not with those of any other series is that the oxidation of phenophthalin by hydrogen peroxide under the accelerating action of blood is like the greater number of chemical processes influenced by temperature; the rate of oxidation increasing, within certain limits at least, with rise of temperature, this effect being most noticeable for short intervals of time. That such is the case may be seen from the following observations:

Solutions were prepared containing 2 c. c. of the dilute solution of Amoss' blood (normal), containing 1 cu. mm. of blood in 250 c. c. and 5 c. c. of the reagent. Glass-stoppered bottles containing these solutions were kept at 2° C., 14° C., and 39° C., for fifteen minutes and one hour, respectively, at the end of which time the color of the several solutions was compared with that of a standard solution of phenolphthalein in N/10 sodium hydroxide. The standard was arbitrarily set at 5 divisions on the scale of the colorimeter. The follow-

ing readings were obtained for these several solutions at the temperatures and intervals indicated above:

Time.	Temperature.	Readings on colorimeter scale.	Standard.
	°C.		
15 minutes.....	2	10.5	5
Do	14	4.6	5
Do	39	3.1	5
1 hour	2	3.8	5
Do	14	2.8	5
Do	39	3.6	5

It will be observed, therefore, especially for the shorter interval, that a rise of temperature causes an increase in the amount of phenolphthalin oxidized, the apparently low result reached at 39° C. for one hour being due to a gradual fading out of color of the phenolphthalein in alkali, a change which also probably takes place more rapidly with rise of temperature and which will be more fully discussed in a subsequent portion of this communication. Up to this time our experiments have been carried on at room temperature which has varied within a range of ten degrees or more, during the time that this investigation has been in progress. Hence, we see that only the results of any one series of experiments are strictly comparable among themselves, for the reason that it has proven practicable to carry out only one series of experiments at any particular time and day.

Up to the present time the peroxidase activity of the blood of forty-seven different persons has been determined in the manner above described with the following results:

SERIES NO. 1.

Date.	Name of person.	Condition.	Per cent of hemoglobin.	Colorimeter readings at the end of 24 hours compared with standard phenolphthalein solution No. 1, ^a set at 5 divisions on the colorimeter scale.	Quantity of phenolphthalein formed, in milligrams. ^b	Quantity of phenolphthalin oxidized, in milligrams.	Per cent oxidized	Oxidizing power of the blood, in terms of normal = 100.
Apr. 22	Amoss	Normal.....	96	3.4	0.468	0.471	29.4	100
22	Collier	Pernicious anemia ...	20-21	19.5	.0816	.082	5.1	17
22	Hynsondo	27	11.6	.137	.138	8.6	29

SERIES NO. 2.

Apr. 24	Amoss.....	Normal.....	96	6.6	0.24	0.242	15.1	100
24	Callahan.....	Fibroma, uterus.....	31	21.75	.0731	.074	4.6	30.4
24	Johnson	Disease unknown	49	12.5	.127	.128	8	53

^aStandard phenolphthalein solution No. 1 contained 0.0318 gram phenolphthalein in 100 c. c. alcohol. 1 c. c. of this solution measured out by pipette in usual manner and mixed with 5 c. c. of distilled water and 1 c. c. N/10 sodium hydroxide furnished the standard for the color comparison.

^bThe quantity of phenolphthalein formed in milligrams and the quantity of phenolphthalin oxidized, also in milligrams, has been calculated in the following manner: As already pointed out, 5 c. c. of the phenolphthalin reagent was used throughout the work. This reagent contained 0.032 gram of phenolphthalin in 100 c. c. of the solution; 1 c. c. of the reagent contained 0.00032 gram of phenolphthalin, and 5 c. c. contained $0.00032 \times 5 = 0.0016$ gram of phenolphthalin. If this were completely oxidized, it would yield 0.00159 grams of phenolphthalein. The standard solutions of phenolphthalein employed in making the color comparisons all contained 0.0318 gram of phenolphthalein in 100 c. c. of solution. Hence, 1 c. c., the amount employed in making up the standard for the color comparison, contained 0.000318 gram of phenolphthalein or one-fifth of the amount of phenolphthalein which would have been formed had all of the phenolphthalin employed in each test been oxidized. In making the color comparisons in the colorimeter, the colorimeter scale on the side of the standard was arbitrarily placed at 5 divisions and the other scale adjusted until the colors matched on the two sides of the instrument. If, now, in order to match the standard, which had been set at 5, the other scale should have had to be placed at 5, then the color of the solution originally would have been exactly equal to that of the standard or to the color produced by 0.000318 gram of phenolphthalein, or 0.318 milligram of phenolphthalein would have resulted from the oxidation. Had it been necessary to set the scale of the test at 1 in order to match the standard at 5, then, obviously, five times the amount of phenolphthalein present in the standard, or $0.000318 \times 5 = 0.00159$ gram, or 1.59 milligrams, would have been formed.

Hence, in order to calculate the amount of phenolphthalein formed during these experiments we have from the foregoing the following proportions:

$$5 : 5 :: .000318 : x$$

and

$$1 : 5 :: .000318 : x$$

from which it follows that the amount of phenolphthalein formed is equal to 0.00159 divided by the reading on the colorimeter scale, when the standard is set at 5 on the same scale, and since

$$318 : 320 :: 1 : 1.006$$

we multiply the number of milligrams of phenolphthalein formed by 1.006 in order to get the amount of phenolphthalin oxidized in milligrams.

To take the first case under Series No. 1, April 22, the colorimeter reading was 3.4 in terms of the standard=5. Hence, to calculate the amount of phenolphthalein formed, we would have:

$$\frac{0.00159}{3.4} = .000468 \text{ or } 0.468 \text{ milligrams}$$

and for the phenolphthalin oxidized:

$$0.468 \times 1.006 = 0.471.$$

(See Series No. 1, Apr. 22.)

SERIES NO. 3.

Date.	Name of person.	Condition.	Per cent of hemoglobin.	Colorimeter readings at the end of 24 hours compared with standard phenolphthalein solution No. 2, ^a set at 5 divisions on the colorimeter scale.	Quantity of phenolphthalein formed, in milligrams.	Quantity of phenolphthalein oxidized, in milligrams.	Per cent oxidized.	Oxidizing power of blood, in terms of normal = 100.
Apr. 25	Amoss.....	Normal.....	107	4.6	0.346	0.348	21.8	100
25	Edna.....	Broncho-pneumonia	28	25	.064	.0644	4.02	19
25	Thomas.....	Disease unknown	42	13.6	.117	.118	7.4	34
25	Antony.....	do.....	22	31.5	.0505	.0508	3.2	15
25	Teddy.....	do.....	44	13.2	.121	.122	7.6	35

SERIES NO. 4.

Apr. 26	Amoss.....	Normal.....	107	3.8	0.42	0.423	26.4	100
26	Carl.....	Disease unknown	43	9.2	.173	.177	11.1	42
26	Irvine.....	do.....	82.5	4.4	.361	.363	22.7	86
26	T. Tanner.....	Slight anemia.....	75	5.1	.311	.313	19.6	74

^aStandard phenolphthalein solution No. 2 same as No. 1, except that the solution was made up with water and alcohol. On standing it deposits phenolphthalein, and hence can not be kept for more than a few days at a time.

SERIES NO. 5.

Date.	Name of person.	Condition.	Per cent of hemoglobin.	Colorimeter readings at the end of 24 hours compared with standard phenolphthalein solution No. 3, ^a set at 5 divisions on the colorimeter scale.	Quantity of phenolphthalein formed, in milligrams.	Quantity of phenolphthalein oxidized, in milligrams.	Per cent oxidized.	Oxidizing power of blood, in terms of normal = 100.
May 3	Amoss.....	Normal.....	103	2.65	0.6	0.604	37.8	100
3	Seboure.....	do.....	100	2.5	.636	.64	40	105
3	Beavers.....	do.....	88	3	.53	.533	33.3	88
3	Porch.....	do.....	92	2.8	.569	.571	35.6	94
3	Murray.....	do.....	86	3	.53	.533	33.3	88
3	Schrader.....	do.....	90	2.8	.568	.571	35.6	94

SERIES NO. 6.

May 7	Amoss.....	Normal.....	97	2.1	0.757	0.762	47.6	100
7	Comber.....	Fibroma, uterus.....	54	4	.398	.401	25.1	53
7	Cline.....	Typhoid fever.....	77	3.5	.454	.457	28.5	59.5
7	Carrolli.....	Empyema.....	79	3.3	.481	.484	30.2	63

^aStandard phenolphthalein solution No. 3 same as No. 2, except that it contained a larger proportion of alcohol. It also deposited phenolphthalein after long standing.

SERIES NO. 7.

Date.	Name of person.	Condition.	Per cent of hemo-globin.	Colorimeter readings at the end of 24 hours compared with standard phenolphthalein solution No. 4, ^a set at 5 divisions on the colorimeter scale.	Quantity of phenolphthalein formed, in milligrams.	Quantity of phenolphthalein oxidized, in milligrams.	Per cent oxidized	Oxidizing power of blood, in terms of normal =100.
May 9	Geo. Bunay	Typhoid fever.....	88	6.1	0.26	0.262	16.4	70
9	R. Somax	Typhoid fever convalescent.	73.5	7.5	.212	.213	13.3	57
9	Ger. Rossier.....	Hemorrhage from miscarriage.	67	6.3	.252	.254	15.9	67
9	R. Russ	Pelvic cyst	83	5	.318	.32	20	86
9	L. Grant	Suspected tuberculosis.	66	6.4	.248	.25	15.6	66
9	G. Saunders.....	Menorrhagia	67	5.9	.27	.272	17	73
9	R. Spencer.....	Disease of kidneys....	100	3.4	.467	.47	29.4	126
9	M. Foster	General sepsis	52	9.4	.169	.17	10.6	45.5
9	Amoss	Normal.....	97	4.3	.37	.372	23.3	100

SERIES NO. 8.

May 10	McIntyre	Tuberculosis and heart disease.	84	4.8	0.331	0.333	20.8	92
10	D. Murphy	Typhoid fever.....	80	5.6	.283	.285	17.8	79
10	G. Corlee.....	Acute rheumatism ...	61	7.3	.218	.219	13.7	61
10	Mrs. Aley	Tuberculosis	79	5.45	.291	.293	18.3	81
10	Amoss	Normal.....	97	4.45	.357	.359	22.4	100

SERIES NO. 9.

May 22	L. Shepherd.....	Healthy child	90	6.4	0.248	0.25	15.6	74.3
22	Mrs. Shepherd ..	Not normal.....	84	5.5	.29	.292	18.2	86.6
22	Mrs. Kastic	Normal.....	91	4.7	.338	.34	21.2	101
22	Dr. Shepherd....	Not normal.....	79	6.2	.256	.258	16.1	76.6
22	Amoss	Normal.....	100	4.75	.335	.337	21	100
22	Water control...	None,	(b)	None.	None.	None.	None.

SERIES NO. 10.

June 4	R. Hickey	Wound in knee.....	99	4.2	0.38	0.382	23.9	110
4	S. Lafero.....	Abdominal cyst	86	6.6	.241	.243	15.2	70
4	J. Reeves.....	Uterine fibroma	35	19.3	.082	.0825	5.1	23.5
4	Alice Kinsley ...	Shingles.....	81	5.5	.29	.292	18.2	83.8
4	E. Mason.....	Tuberculosis	71	7.3	.22	.221	14.8	68.2
4	Amoss	Normal.....	90	4.6	.345	.347	21.7	100
4	Amoss (June 2)do	99	4.7	.328	.34	21.2	97.7

^aStandard phenolphthalein solution No. 4 was prepared by dissolving 0.0318 gram of phenolphthalein in absolute alcohol and making up to 100 c.c. with absolute alcohol; 1 c.c. of the solution measured out in pipettes by Rosenau's method and mixed with 5 c.c. water and 1 c.c. N/10 sodium hydroxide gave the standard for the color comparison, and was employed in all subsequent parts of the work, unless expressly stated to the contrary.

^bColorless.

Date.	Name of person.	Condition.	Per cent of hemoglobin.	Colorimeter readings at the end of 24 hours compared with standard phenolphthalein solution No. 4, set at 5 divisions on the colorimeter scale.	Quantity of phenolphthalein formed, in milligrams.	Quantity of phenolphthalein oxidized, in milligrams.	Per cent oxidized.	Oxidizing power of blood, in terms of normal =100.
June 5	M. Rawles.....	Child 10 days old.....	87	7.3	0.22	0.221	14.8	82.2
5	K. Riley	Hemorrhoids and abdominal cyst.	70	13.1	.121	.122	7.5	42.2
5	G. Bunay.....	Typhoid convalescent	89	8.6	.185	.186	11.6	64.4
5	Wm. Pryor.....	Tuberculosis of hip joint.	36	20.6	.077	.0775	4.84	27
5	Ellen Lehr.....	General tuberculosis	49	9	.177	.178	11.1	61.6
5	Amoss	Normal.....	86	5.6	.284	.286	18	100

It is evident, from these results, that in diseased conditions the blood shows a considerable falling off in peroxidase activity, or oxygen-carrying power, as compared with that in normal conditions of health, and that in the majority of instances, at least, the peroxidase activity of blood is proportional to the percentage of hemoglobin. That such is the case may be seen by comparing the numbers given in the last column of our tables, in which the oxidizing power of the several specimens of blood are given in terms of normal blood (Amoss), the oxidizing power of which has arbitrarily been made equal to 100, with the several percentages of hemoglobin which are to be found in another column of the tables. It will be observed that in 29 out of the 47 specimens examined the numerical agreement between the oxidizing power of the blood and the percentage of hemoglobin is almost numerically exact, and that in the remaining cases it is sufficiently close to indicate a general agreement and correlation between oxidizing power and hemoglobin content.

The greatest differences in oxidizing power of the several samples of blood were brought out by allowing the oxidation to proceed for twenty-four hours. In most cases, however, if not in all, differences of a similar nature were shown after much shorter intervals. Thus, with the bloods composing series No. 1, which were examined on April 22, the following results were obtained for several intervals, three of which were shorter than twenty-four hours. (See Table No. 1.)

TABLE NO. 1.

[Series No. 1 (for several intervals).]

Date.	Name of person.	Condition.	Per cent of hemo-globin.	Colorimeter readings at the end of intervals indicated compared with standard phenolphthalein solution, set at 5 divisions on the colorimeter scale.				Quantity of phenolphthalein formed, in milligrams, during the several intervals.			
				5 min-utes.	15 min-utes.	1 hour.	24 hours	5 min-utes.	15 min-utes.	1 hour.	24 hours.
Apr. 22	Amoss..	Normal.....	96	8.75	3.3	2.6	3.4	0.182	0.481	0.612	0.468
22	Collier..	Pernicious anemia.	20-21	16.5	8.8	8.45	19.5	.096	.181	.188	.0816
22	Hynson.do.....	27	16.5	7.2	6.1	11.6	.096	.221	.261	.137

Date.	Name of person.	Quantity of phenolphthalin oxidized, in milligrams, during the several intervals.				Percentage of oxidation during the several intervals.			
		5 min-utes.	15 min-utes.	1 hour.	24 hours.	5 min-utes.	15 min-utes.	1 hour.	24 hours.
Apr. 22	Amoss....	0.183	0.484	0.616	0.471	11.4	30.2	38.5	29.4
22	Collier....	.097	.182	.189	.082	6	11.3	11.8	5.1
22	Hynson...	.097	.222	.263	.138	6	14	16.4	8.6

FADING OF THE PHENOLPHTHALEIN COLOR.

Reference has already been made to the fact that the color of the phenolphthalein solution resulting from the oxidation of phenolphthalin by hydrogen peroxide under the influence of minute quantities of blood gradually fades somewhat, so that apparently the quantity of phenolphthalin oxidized at the end of twenty-four hours is less than the amount oxidized during one hour.

That such is the case is evident from the results given in Table No. 1. An examination of these results shows an increase in the amount of oxidation up to the end of one hour, after which a gradual fading of the color of the solution occurs until, at the end of twenty-four hours, the amount of phenolphthalin oxidized is apparently from one-quarter to one-half less than the amount oxidized at the end of one hour. Without it is that the blood contains a substance capable of reducing phenolphthalein—and this, of course, is conceivable—it is difficult to see why less phenolphthalin should be oxidized at the end of twenty-four hours than at the end of one hour. As a matter of fact the fading out of the phenolphthalein color seems to depend upon several causes.

In the first place, it seems to depend upon the character of the blood, being greater and more rapid in the case of diseased bloods, poor in hemoglobin. The result is that the most striking differences between normal and diseased bloods are revealed after the longer

interval of time, this condition apparently resulting from a difference in oxidizing power in the first place, and also from a difference in the conduct of the blood toward phenolphthalein in alkali after this substance has been once formed.

In the second place, as is well known, a large excess of alkali destroys the colored substance first formed by the action of alkali on phenolphthalein by the formation of a colorless salt. The rate of decomposition of the colored compound of phenolphthalein and alkali seems to depend entirely on the concentration of the alkali. With large amounts of alkali the colored compound is destroyed immediately; with greater dilution and smaller amounts of alkali the colored compound is decomposed more slowly and gradually. That it gradually disappears from such a solution, however, may be seen from the following observations.

In order to determine the effect of increasing amounts of sodium hydroxide on the color of phenolphthalein, five solutions were prepared, each containing 0.318 milligram of phenolphthalein in 1 c. c. of absolute alcohol and 1, 2, 3, 4, and 5 c. c. N 10 sodium hydroxide, together with sufficient water to make the total volume up to 7 c. c. in each case. The color of these solutions was then compared with that of a phenolphthalein standard, containing 0.318 milligram in 1 c. c. absolute alcohol, 1 c. c. N 10 sodium hydroxide, and 5 c. c. of water, the standard being set at 5 divisions on the colorimeter scale.

The following readings were obtained for the several solutions immediately and after twenty-four hours, the comparison being made with freshly prepared standard in each case.

READINGS ON COLORIMETER.

Quantity of sodium hydroxide N/10	Immediately.	After 24 hours.	Standard.
c. c.			
1	4.9	8.7	5
2	4.95	16.1	5
3	5.4	22.75	5
4	Lost.	Lost.	5
5	13.4	22.6	5

Even at a dilution five times as great as that employed in the above series of experiments, viz, with N 50 sodium hydroxide, the color of phenolphthalein in alkali shows a tendency to fade on standing, but by no means so rapid and pronounced as with N 10 sodium hydroxide. Five solutions were prepared, each containing 0.318 milligram phenolphthalein in 1 c. c. absolute alcohol, and 1, 2, 3, 4, and 5 c. c. N 50 sodium hydroxide and sufficient water to make the total volume of the several solutions up to 7 c. c. in each case. These were compared with a fresh standard solution of phenolphthalein containing 0.318 milli-

gram of phenolphthalein in 1 c. c. of absolute alcohol, 1 c. c. N 10 sodium hydroxide, and 5 c. c. of water, immediately and after twenty-four hours, with the following results:

READINGS ON COLORIMETER.

Quantity of sodium hydroxide N/50.	Immediately.	After 24 hours.	Standard.
c. c.			
1	5	6	5
2	5	6.2	5
3	4.8	7.5	5
4	5	7.7	5
5	4.9	9.3	5

Similar experiments were tried using N 500 sodium hydroxide in the proportion of 1, 2, 3, 4, and 5 c. c. at a total dilution of 7 c. c. The following results were obtained on comparison with the phenolphthalein standard employed in the previous series of experiments:

READINGS ON COLORIMETER.

Quantity of sodium hydroxide N 500.	Immediately.	After 24 hours.	Standard.
c. c.			
1	12	Colorless.	5
2	6.5	8.8	5
3	5.5	6.4	5
4	5.5	5.9	5
5	5	5.9	5

It would seem, therefore, that, so far as the influence of alkali on the fading of the phenolphthalein color is concerned, the most rapid fading occurs either with very small or with very large amounts of alkali. With very small amounts of alkali the fading out of the color is doubtless due to the absorption of carbon dioxide from the air in sufficient amounts to decompose the colored salt, and in the case of larger amounts of alkali the fading is probably connected with the formation of a colorless salt-like body from the colored quinoid substance. Regardless of any theory of the process, the fact remains that the presence of alkali may be responsible for the fading out of the phenolphthalein color encountered in our own experiments with blood.

Still, a third factor involved in the fading of the phenolphthalein color is the presence of hydrogen peroxide. That such is the case, is indicated by the fact that in those experiments in which blood alone is employed to effect the oxidation of phenolphthalein in alkaline solution, the depth of color persists unchanged for a much longer interval of

time than when hydrogen peroxide is present, and yet the other conditions of the experiments are essentially the same, except that slightly larger amounts of blood are employed in effecting the oxidation and slightly more phenolphthalein is formed as the result of the oxidation, and hydrogen peroxide is absent, or if present, only as a minute impurity in the reagents employed. Otherwise the general conditions of the experiments are the same in the two cases, and the same amount of sodium hydroxide is present at the same concentration.

It is more than likely, therefore, that the gradual fading out of the phenolphthalein color is not due entirely to any one of the three factors enumerated in the foregoing, but rather to a combination of causes, the complete effect of which it is impossible to picture at the present stage of this investigation.

Suffice it to say in this connection, however, that this phenomenon in nowise invalidates either our results or the deductions therefrom.

THE DIRECT OXIDATION OF PHENOLPHTHALIN BY BLOOD IN ALKALINE SOLUTION.

Reference has already been made to the fact that in alkaline solution phenolphthalin is directly oxidized by blood without the intervention of hydrogen peroxide. It therefore occurred to us to make a few measurements of the direct oxidizing power of a number of specimens of blood from different individuals with the view of noting any possible variations that might exist among the several specimens in health and disease.

Somewhat larger amounts of blood are required to effect the oxidation than when hydrogen peroxide is present. Accordingly in this series of experiments 1 cubic millimeter of blood was diluted to 100 c. c. with distilled water. Two cubic centimeters of this solution were then brought together with 5 c. c. of a reagent containing 0.032 gram of phenolphthalin and 21 c. c. N/10 sodium hydroxid at a total dilution of 100 c. c.

These mixtures were allowed to stand in glass-stoppered bottles for the several intervals of time recorded in Table No. 2, at the end of which the amount of phenolphthalein formed as the result of the oxidation was determined colorimetrically by comparison in the colorimeter with standard solution of phenolphthalein No. 4. The results of these measurements are given in Table No. 2.

TABLE NO. 2.

Series.	Date.	Name of person.	Condition.	Per cent of hemo- globin.	Colorimeter readings at the end of in- tervals indicated compared with standard phenolphthalein solution, set at 5 divisions on the colorimeter scale.							
					1 hour.	2 hours.	24 hours.	48 hours.	72 hours.	96 hours.	120 hours.	168 hours.
1	June 2	Amoss	Normal	99	21.8	1.60	1.55	1.6	2
		Porch	do.	95	21.4	1.50	1.50	1.6	1.6
		Schrader	do.	94	22	1.55	1.50	1.95	1.9
		Control (water)	(a)	(b)	(b)
2	June 4	Amoss (June 2)...	Normal	99	16	1.7	1.5	1.7	2.1	2.7	3.6
		Amoss (June 4)...	do.	90	16	1.8	1.5	1.6	1.9	2.4	3.7
		Robt. Hickey.....	Fracture wound in knee.	99	15.8	1.8	1.5	1.7	1.7	2.5	3.1
		S. Lafero.....	Abdominal cyst.....	86	16	1.7	2.1	2.1	2.4	3	4.1
		J. Reeves.....	Uterine fibroma.....	35	27.4	3.7	3.3	4.3	4.8	6.7	8.9
		Alice Kinsley	Shingles	81	16.6	1.9	1.9	1.8	2.2	2.9	5
		Edith Mason	Tuberculosis	71	17.4	1.9	2.2	2.3	2.7	3.1	4.8
		Control (water)	(a)	(a)	(b)	(b)
3	June 5	Amoss	Normal	86	21	1.6
		M. Rawles.....	Child 10 days old	87	23.4	1.6
		K. Riley	Hemorrhoids and ab- dominal cyst.	70	28	2.1
		G. Bunay.....	Typhoid fever, conva- lescent.	89	26	1.9
		Wm. Pryor	Tuberculosis of hip joint.	36	42	2.9
		Ellen Lehr	General tuberculosis..	49	33.4	2.4
4	June 6	Rowze.....	Fracture of skull.....	83	14	1.6	1.6	1.5	2.8
		M. Rowze	Labor—childbirth	54	19.2	1.9	2.2	2.5	4.2
		Amoss.....	Normal	90	14.2	1.55	1.55	1.6	2.5

Series.	Date.	Name of person.	Quantity of phenolphthalein formed, in milligrams, during the several intervals.							
			1 hour.	2 hours.	24 hours.	48 hours.	72 hours.	96 hours.	120 hours.	168 hours.
1	June 2	Amoss	0.073	0.934	1.02	0.994	0.795
		Porch074	1.06	1.06	.994	.994
		Schrader.....	.072	1.02	1.06	.85	.840
2	June 4	Amoss (June 2)	0.099	.93	1.06	.93	.76	0.59	0.41
		Amoss (June 4)099	.88	1.06	.994	.84	.66	.43
		Robt. Hickey100	.88	1.06	.93	.93	.64	.51
		S. Lafero099	.93	.76	.76	.66	.53	.39
		J. Reeves058	.43	.48	.37	.33	.24	.18
		Alice Kinsley.....095	.84	.84	.88	.72	.55	.32
		Edith Mason.....091	.84	.72	.69	.59	.51	.33
		Control (water)
3	June 5	Amoss076	.994
		M. Rowles068	.994
		K. Riley057	.76
		G. Bunay061	.84
		Wm. Pryor.....038	.55
		Ellen Lehr.....047	.66
4	June 6	Rowze994	.994	1.0656
		M. Rowze.....84	.72	.6438
		Amoss	1.02	1.02	.99464

a None.

b Very faint pink.

TABLE No. 2—Continued.

Series.	Date.	Name of person.	Quantity of phenolphthalin oxidized, in milligrams, during the several intervals.							
			1 hour.	2 hours.	24 hours.	48 hours.	72 hours.	96 hours.	120 hours.	168 hours.
1	June 2	Amoss	0.0735	1	1.03	1	0.81
		Porch075	1.07	1.07	1	1
		Schrader.....	.073	1.03	1.07	.86	.85
2	June 4	Amoss (June 2)	0.10	.94	1.07	.94	.77	0.60	0.45
		Amoss (June 4)10	.89	1.07	1	.85	.67	.44
		Robt. Hickey.....10	.89	1.07	.94	.94	.65	.52
		S. Lafero10	.94	.77	.77	.67	.54	.40
		J. Reeves.....058	.433	.49	.372	.332	.24	.18
		Alice Kinsley096	.85	.85	.89	.73	.56	.32
		Edith Mason092	.85	.73	.70	.60	.52	.332
		Amoss077	1
3	June 5	M. Rawles.....069	1
		K. Riley.....058	.77
		G. Bunay.....062	.85
		Wm. Pryor0382	.56
		Ellen Lehr.....0473	.67
		Rowze	1	1	1.0756
4	June 6	M. Rowze85	.72	.65382
		Amoss	1.03	1.03	165

Series.	Date.	Name of person.	Percentage of oxidation during the several intervals.								Oxidizing power of blood in terms of normal. (Amoss)=100. (24-hour interval.)
			1 hour.	2 hours.	24 hours.	48 hours.	72 hours.	96 hours.	120 hours.	168 hours.	
1	June 2	Amoss	4.6	62.5	64.4	62.5	50.6	100
		Porch	4.7	66.9	66.9	62.5	62.5	107
		Schrader	4.5	64.4	66.9	53.7	53.1	103
2	June 4	Amoss (June 2).....	6.25	58.7	66.9	58.7	48.7	37.5	28.1	94
		Amoss (June 4).....	6.25	55.6	66.9	62.5	53.1	42	27.5	89
		Rob't Hickey.....	6.25	55.6	69.9	53.7	58.7	40	32.5	89
		S. Lafero.....	6.25	58.7	48.7	48.7	42	33.7	25	94
		J. Reeves.....	3.61	27	30.6	23.2	20	15	11.25	43
		Alice Kinsley.....	6	53.1	53.1	55.6	45.6	35	20	85
		Edith Mason	5.75	53.1	45.6	43.7	37.5	32.5	20.7	85
3	June 5	Amoss	4.8	62.5	100
		M. Rawles.....	4.3	62.5	100
		K. Riley.....	3.6	48.7	78
		G. Bunay.....	3.9	53.1	85
		Wm. Pryor.....	2.4	35	56
		Ellen Lehr	2.9	42	67
4	June 6	Rowze.....	62.5	62.5	66.9	35	100
		M. Rowze	53.1	45.6	40	24	85
		Amoss	64.4	64.4	62.5	40	103

A consideration of these results shows that even though a relatively larger amount of blood is present in the solution, the oxidation proceeds much more slowly than when hydrogen peroxide is also present. When hydrogen peroxide is present normal blood, at a dilution of

1 cu. mm. to 250 c. c., can oxidize 38.5 per cent of the phenolphthalin present in one hour; whereas blood alone, at a dilution of 1 c. mm. to 100 c. c. acting in the presence of alkali, is only able to oxidize 4.6 per cent of the phenolphthalin in the same time. When hydrogen peroxide is present the maximum of oxidation is reached in one hour; whereas in blood alone the maximum is reached only after twenty-four hours.

Secondly, as already pointed out in the foregoing, it is evident that when blood alone is employed to effect the oxidation of the phenolphthalin the depth and intensity of the phenolphthalein color persists unchanged for a much longer time than when hydrogen peroxide is present. For example, with normal blood the color remains undiminished for seventy-two hours or even longer; whereas with the blood of diseased persons the fading takes place somewhat more rapidly. On the other hand, it will be recalled in this connection that when hydrogen peroxide is present the color of the phenolphthalein fades considerably, even in twenty-four hours, and, in fact, often in even less time. Hence, as already pointed out, it would seem that one of the causes of the fading of the phenolphthalein color is the presence of hydrogen peroxide.

Another point of interest in this connection and one that requires still further investigation is that in no case here studied, either with or without hydrogen peroxide, is the phenolphthalin completely oxidized, the maximum oxidation with blood alone being 66.9 per cent and with blood and hydrogen peroxide 47.6 per cent. This either indicates an insufficiency in available oxygen or it may be associated with the fading of the phenolphthalein color.

Thirdly, it will be observed that the direct oxidizing power of the blood of fifteen persons has been determined for twenty-four hours. In the last column of the table will be found the oxidizing power of these several specimens of blood calculated in terms of normal blood (viz, that of Amoss), arbitrarily made equal to 100. A comparison of these numbers among themselves and with the percentages of hemoglobin of the several specimens reveals much the same relationship that has been found to exist between peroxidase activity and per cent of hemoglobin, viz, the former is proportionate to the quantity of hemoglobin present in blood. So here the higher the hemoglobin content the greater the direct oxidizing power of blood. Out of the fifteen specimens whose direct oxidizing power has been determined eight have been found to contain hemoglobin varying from 83 to 99, and eleven have been found to have a direct oxidizing power varying from 85 to 107. Four of these bloods were markedly low in percentage of hemoglobin, the quantity varying from 35 to 54 per cent and three have been found to have a low direct oxidizing power varying from 43 to 67.

As a general thing the numbers for the direct oxidizing power of these several specimens of blood in terms of normal blood (Amoss, equal to 100) are somewhat higher than the corresponding numbers for the percentages of hemoglobin. This is true in twelve out of the fifteen cases studied.

On account of the scarcity of clinical material we have not yet been able to subject this method to the rigorous test which is required before we shall be able to say whether such examinations as those herein described will have any practical value as aid to diagnosis. From the comparatively few cases, however, that we have thus far been able to collect there is every indication that such will prove to be the case. We propose, therefore, to extend these observations as rapidly as the necessary clinical material can be obtained and at the same time we shall endeavor to perfect and simplify the methods above described for determining the activity of the blood as a carrier of oxygen.

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TREASURY DEPARTMENT.

Public Health and Marine-Hospital Service of the United States.

WALTER WYMAN, Surgeon-General.

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M. J. ROSENAU, Director.

October, 1906.

A STOMACH LESION IN GUINEA PIGS CAUSED BY DIPHTHERIA TOXINE

AND ITS BEARING UPON

EXPERIMENTAL GASTRIC ULCER.

BY

M. J. ROSENAU

AND

JOHN F. ANDERSON.



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A STOMACH LESION IN GUINEA PIGS CAUSED BY DIPHThERIA TOXINE, AND ITS BEARING UPON EXPERIMENTAL GASTRIC ULCER.^a

By MILTON J. ROSENAU,

Passed Assistant Surgeon, Director Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service,

and

JOHN F. ANDERSON,

Passed Assistant Surgeon, Assistant Director Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service.

Guinea pigs dying acutely from injections of diphtheria toxine frequently show a lesion in the stomach which, so far as we know, has not been described.

Our attention was first called to the condition of the stomachs of guinea pigs used in our diphtheria work by Assistant Surgeon A. M. Stimson in the summer of 1905. Since that time we have collected from our autopsy records 2,882 protocols in which the condition of the stomach was noted. Of these, 1,897 guinea pigs, or 66 per cent, showed the lesion in the stomach described in this bulletin.

In the many thousand autopsies upon guinea pigs used in this laboratory in preparing the standard unit for measuring the strength of diphtheria antitoxin and also for verifying the potency of antidiphtheric serum made by the licensed manufacturers, we constantly see the lesions usually found in animals dying from diphtheria poisoning, such as darkened and congested adrenals, effusions into the pleura and other serous cavities, local edema, necrosis and hemorrhagic reaction at the site of inoculation, etc.; but it is difficult to understand how the condition of the mucosa of the stomach, which is so very evident in a large proportion of the guinea pigs, has so long escaped observation.

This lesion may perhaps assume practical importance in view of the light it may throw upon experimental gastric ulcer.

^a Manuscript submitted for publication July 26, 1906.

The experimental production of true gastric ulcer, simulating the so-called peptic or round ulcer in man, has met with little success. The following table of experiments by previous investigators, taken from Turck's article upon ulcer of the stomach in the Journal of the American Medical Association, volume 46, June 9, 1906, page 1753, gives in condensed form the method used to produce experimental gastric ulcer and results obtained:

TABLES OF EXPERIMENTS BY PREVIOUS INVESTIGATORS.

A. MECHANICAL AND PHYSICAL INJURY.

	Result.
Ritter. Violent bruises.	
Decker. Heat	Ulcer.
Matthes. Trauma (with 5 per cent HCl)	Ulcer.
Schmidt. Trauma (with HCl).	
Körte. Pinching stomach with clamps.	Ulcer.

B. CHEMICAL.

Roth. Crystals of nitrate of silver introduced into stomach.	Ulcer.
---	--------

1. *HCl as a necessary factor.*

Riegel. HCl necessary.	
Matthes. Trauma (without HCl)	Negative.
Trauma (with 5 per cent HCl)	Ulcer.
Schmidt. HCl and trauma.	
Ewald. HCl essential factor.	

2. *Contra HCl.*

Pawlow. Hyperacidity a consequence.	
Du Misinl. Superacidity without significance.	
Ageron. HCl may be persistently absent.	
Kavetsky. Synchronous ulcer of the stomach and bladder.	

C. GENERAL DYSEMIA.

Virchow. Anemia and chlorosis.	
Quincke and Daetwyler. Anemia by producing gradual hemorrhage and local trauma	Ulcer, which healed with difficulty.
Silbermann. Hemoglobinemia	Ulcer.
Futterer. Hemoglobinemia	Ulcer.
Cohnheim. Hemoglobinemia by mechanical injury and injection of laked blood	Ulcers.

D. DISTURBANCE OF LOCAL CIRCULATION.

Virchow. Embolism, thrombi, aneurism, or varicose veins.	
Klebs and Welti. Thrombi.	
Panum. Injection of emulsion of wax into femoral vein.	Gastric infarcts, ulcer.
Talma. Ligation of esophagus and pylorus	Ulcer.
Rindfleisch. Venous stasis; prolonged ischemia.	
Axel Key. Prolonged ischemia, due to contraction of gastric muscle	No experiments.
Müller. Tied portal vein	Ulcer.

E. INJURIES TO NERVES AND NERVE CENTERS.

Schiff-Ebstein.	Intersection of thalami and peduncles.....	Ulcer.
Brown-Sequard.	Anterior corpora quadrigemina.....	Ulcer.
Vidova.	Injection of alcohol into vagus.....	Negative.
Vidova.	Section of the sympathetic.....	Ulcer.
Yzeren.	Section of the sympathetic with section of vagi below the diaphragm.....	Ulcer.
Saitta.	Section of the sympathetic with section of vagi below the diaphragm.....	Ulcer.
Ophüls.	Section of the sympathetic with section of the vagi below the diaphragm.....	Ulcer.
Koch and Ewald.	Section of cord and 5 per cent HCl in stomach.....	Ulcer.

F. LOCAL INFECTION.

Cohnheim.	Injection. Infected suspensions of lead chromate..	Erosions and ulcers.
Böttcher.	Infection as cause of ulcer.....	Opposed by Körte.
Nauwerck.	Infection observed at edge of ulcer.	

Turck, in following the subject further has succeeded in producing ulcers of the stomach and duodenum in dogs by feeding *B. coli communis* for a variable length of time and as a result of his work considers that we now have, for the first time, a firm basis by which to solve the final or underlying etiology of gastric ulcer.

In connection with the lesion in guinea pigs which we describe it is interesting to note that Turck^a attempted the production of gastric ulcer in dogs by the injection of diphtheria toxine into the stomach wall. This, it seemed, did not produce an ulcer, but pinhead hemorrhagic foci in the duodenum or local necroses near the pylorus. When the diphtheria toxine was injected into the mesenteric vessels, Turck also failed to produce ulcer, but obtained necroses in two weeks in the duodenum and near the pylorus.

We find that gastric ulcer may be produced in the guinea pig by the subcutaneous inoculation of diphtheria toxine given in sufficient quantity to cause the acute death of the animal. It follows injections of a minimal lethal dose, as well as the injection of the toxine-antitoxin mixture (L+ dose) used in measuring the strength of diphtheria antitoxin. When the toxine is completely neutralized by the antitoxin, as in the case of the L⁰ mixture, and the animal afterwards killed, the stomach shows no lesion.

The lesion is caused by infection with the diphtheria bacillus as well as by injections of the diphtheria toxine. We injected a number of guinea pigs with a young agar culture of *B. diphtheriæ* well washed to free it of toxine. The animals sickened and died in from four to six days. The autopsy findings, so far as the stomach was concerned, were precisely similar to those seen in animals dead of toxine injections.

^aChicago Pathological Society: Transactions, April, 1903.

So far as we know a similar condition of the stomach in human diphtheria has not been observed.

The lesion in the stomach of the guinea pig consists of a sharply defined area of congestion, hemorrhage, or ulceration, near or at the pyloric extremity. Occasionally the lesion extends half an inch into the duodenum and in a few instances the duodenum itself shows slight injection or congestion, although the stomach remains normal.

The first stage consists principally of a congestion, always in the neighborhood of the pylorus. This is best seen in guinea pigs dying in about twenty-four hours as a result of overpowering doses of diphtheria toxine. When the guinea pig dies later, for instance on the second, third, or fourth day, the lesion is more advanced and consists of hemorrhages into the mucosa followed by destruction of tissue sometimes extending into the muscularis, but in no case has perforation been observed.

It is interesting to know whether guinea pigs that received less than a lethal dose of the diphtheria poison from which they ultimately recovered may have had this stomach lesion. In a few instances in our guinea pigs which died on the twenty-second and twenty-eighth days with paralysis we found old blood-stained areas in the mucosa of the stomach in the region of the pylorus, indicating a healed area.

The lesion is not the result of any particular diphtheria toxine, for we have found that it follows the use of all the various diphtheria toxins, some 25 in number, used in this laboratory.

There is no relation between the source of the guinea pig and the effects of the diphtheria toxine, since we have found this lesion in guinea pigs obtained from four outside sources as well as in those bred in the laboratory.

We have examined a number of healthy guinea pigs from our stock in order to assure ourselves that no other cause than the diphtheria toxine could account for the appearances that we find in the stomachs of guinea pigs.

It will be seen from the following table that when guinea pigs are given an injection of diphtheria toxine sufficient to kill them within twenty-four hours, about half the animals show this lesion. When they die on the third or fourth day, a very much larger proportion of the animals show the lesion. About 75 per cent of the guinea pigs dying between the fourth and fifth days show this lesion, but in guinea pigs dying later than the tenth day the relative number of animals showing this stomach lesion gradually diminishes. Guinea pigs dying of late paralysis practically never showed the acute stomach lesion.

The frequency with which guinea pigs, dead of diphtheria toxine, show the stomach lesion.

Time of death.	Condition.	Number.	Lesions.
			<i>Per cent.</i>
Less than 1 day	{Stomach lesion.....	7	54
	{Stomach normal	6	
Between 1 and 2 days	{Stomach lesion.....	104	62
	{Stomach normal	61	
Between 2 and 3 days	{Stomach lesion.....	833	77
	{Stomach normal	235	
Between 3 and 4 days	{Stomach lesion.....	725	73
	{Stomach normal	254	
Between 4 and 5 days	{Stomach lesion.....	163	52
	{Stomach normal	144	
Between 5 and 6 days	{Stomach lesion.....	35	28
	{Stomach normal	85	
Between 6 and 10 days	{Stomach lesion	28	25
	{Stomach normal	84	
More than 10 days	{Stomach lesion.....	2	1.7
	{Stomach normal	116	
Total	{lesion.....	1,897	a 66
	{normal	985	
		2,882	

a Average.

CONTROLS.

A number of comparisons were made with tetanus toxine and various chemical poisons, but in no instance was there found any similar sharply defined lesion in the pyloric extremity of the stomach.

The stomachs of guinea pigs dead of tetanus toxine appeared quite normal.

The stomachs of guinea pigs dying acutely from strong poisons, such as hydrocyanic acid, chloralcyanhydrin, etc., sometimes show acute hemorrhagic areas either of a diffuse or punctate nature, but in such cases the lesion is not confined to the pyloric end of the stomach.

For the effect of various chemical poisons upon the stomach of guinea pigs we are indebted to Dr. Reid Hunt, Chief of the Division of Pharmacology, Hygienic Laboratory, for the following data upon animals used by him in other lines of research and which serve as our controls:

Hydrocyanic acid.

Five guinea pigs were given subcutaneously from 0.005 to 0.006 mg. of hydrocyanic acid per gram of guinea pig, which caused death in one hour fifteen minutes to six hours twenty-five minutes.

G. P. No. 315 (0.005 mg.). Mucosa and submucosa of anterior and posterior walls of stomach showed large acute hemorrhagic areas. Pylorus apparently normal.

G. P. No. 305 (0.0052 mg.). Stomach showed intense hemorrhage into the mucous membrane. Pylorus apparently normal.

G. P. No. 340 (0.0055 mg.). Mucous membrane of whole of stomach and submucosa intensely hemorrhagic.

G. P. No. 327 (0.006 mg.). Enormous punctate hemorrhagic areas on mucous membrane of greater curvature of stomach.

G. P. No. 365 (0.005 mg.). Mucosa of stomach slightly injected and hemorrhagic.

Chloralcyanhydrin.

Eight guinea pigs were injected subcutaneously with chloralcyanhydrin in quantities varying from 0.0052 to 0.03 mg. per gram, which caused the death of the animals in six hours to sixteen minutes. The stomach in each instance was normal, excepting in the two animals receiving the large amounts, as follows:

G. P. No. 330 (0.025 mg.). Acute hemorrhage of the posterior and anterior walls of the stomach, involving both the mucosa and the serous coats.

G. P. No. 325 (0.03 mg.). Stomach shows numerous hemorrhagic areas.

Strophanthin.

Four guinea pigs were injected subcutaneously with strophanthin in amounts varying from 0.001 to 0.005 mg. per gram, causing the death of the animals in one hour thirty-five minutes to forty-three minutes. In each case the stomach appeared normal.

Strychnine sulphate.

Ten guinea pigs were injected subcutaneously with strychnine sulphate, and others with strychnine sulphate plus alcohol. The amount of strychnine varied from 0.004 mg. to 0.005 mg. per gram; these doses caused the death of the animals in eleven minutes to four hours twenty minutes. Stomach was normal in each instance.

Nitroprussiate of soda.

Three guinea pigs were injected with amounts of nitroprussiate of soda varying from 0.015 to 0.018 mg. per gram, which caused the death of the animals in one hour fifteen minutes to two hours fifteen minutes. The stomach was normal in all three cases.



FIG. 1.—STOMACH SHOWING LESION, MILD GRADE.



FIG. 2.—STOMACH SHOWING LESION, SEVERE GRADE.



FIG. 3.—STOMACH SHOWING LESION, VERY SEVERE.

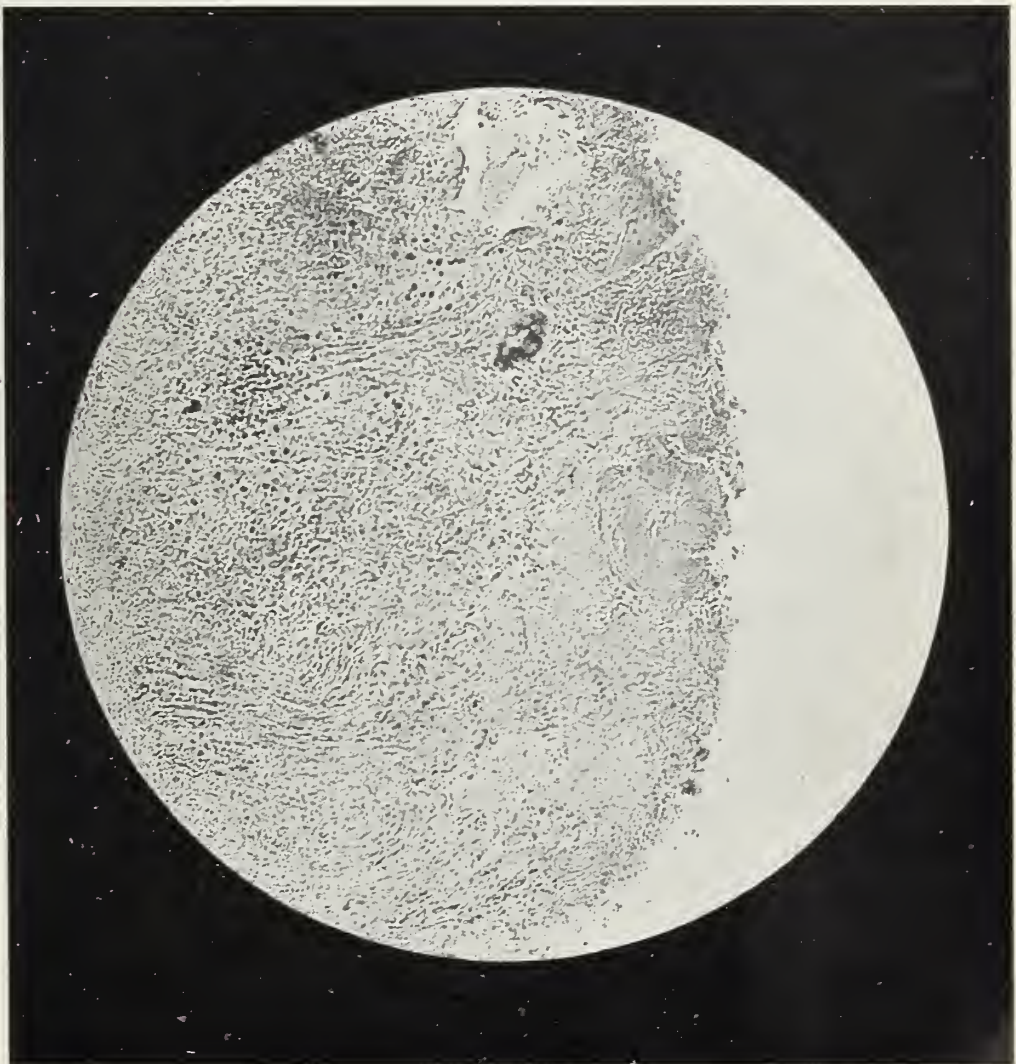


FIG. 4.—COAGULATIVE NECROSIS.

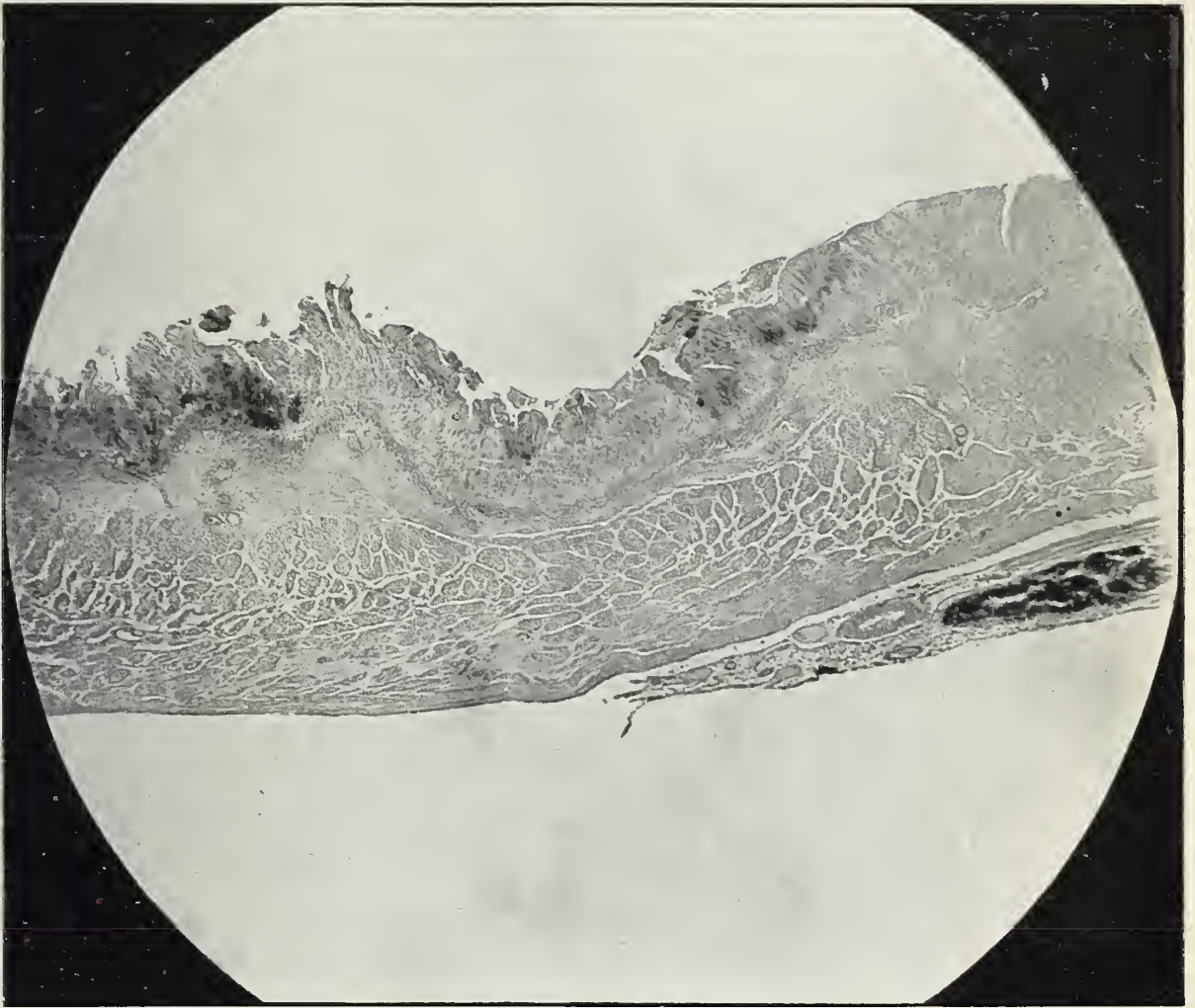


FIG. 5.—CONGESTION AND HEMORRHAGIC AREAS IN MUCOSA.

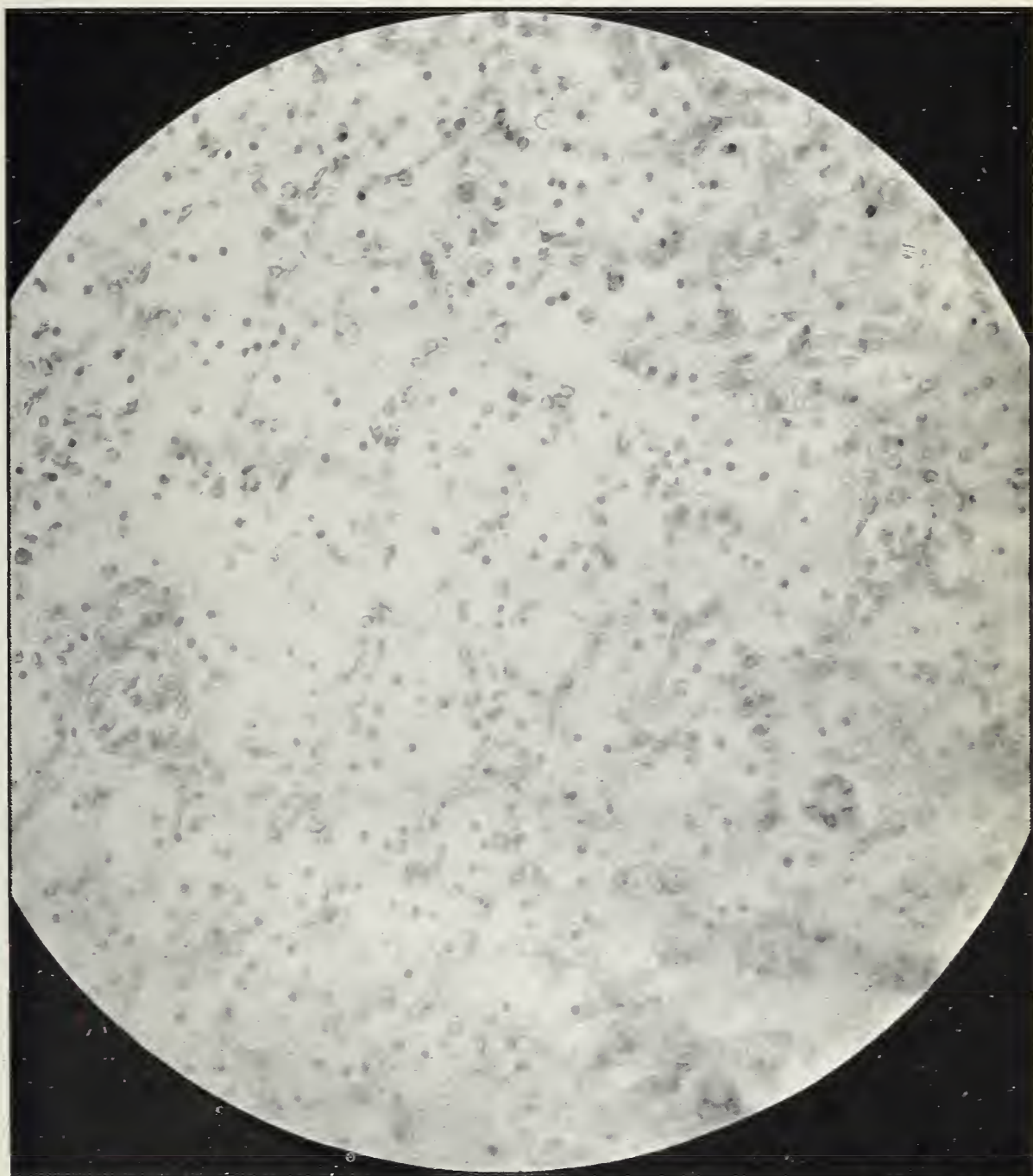


FIG. 6.—CAPILLARY CONGESTION, MUCOSA.

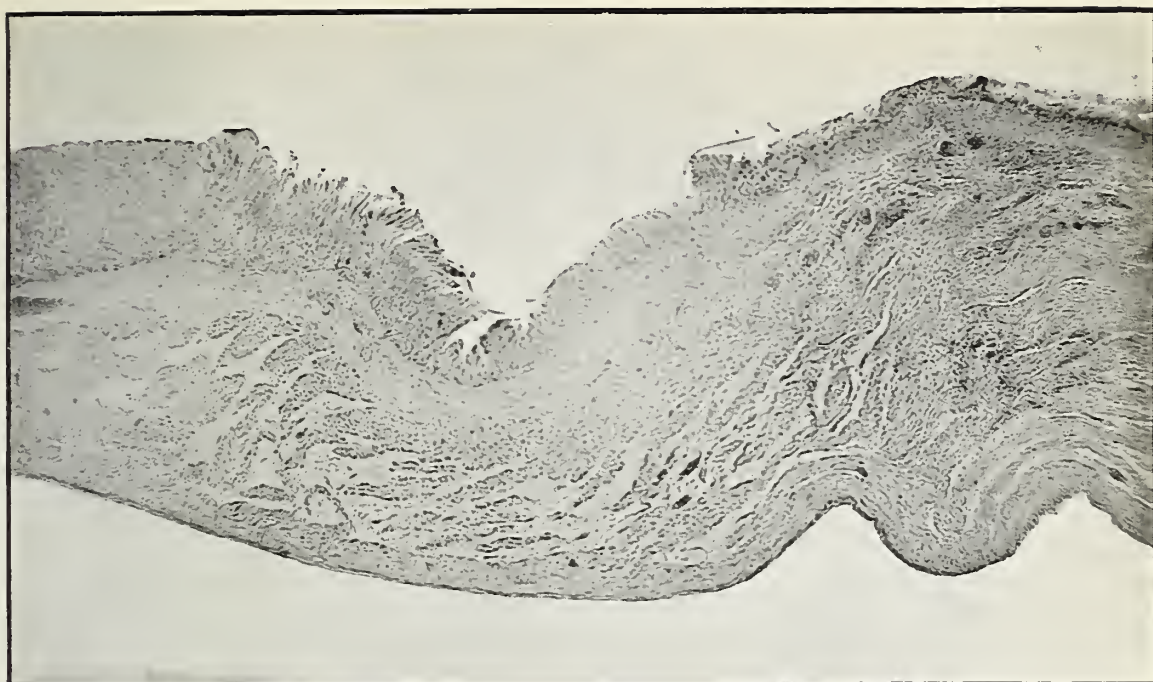


FIG. 7.—ULCER, SHOWING SHARP LINE OF DEMARCATION.

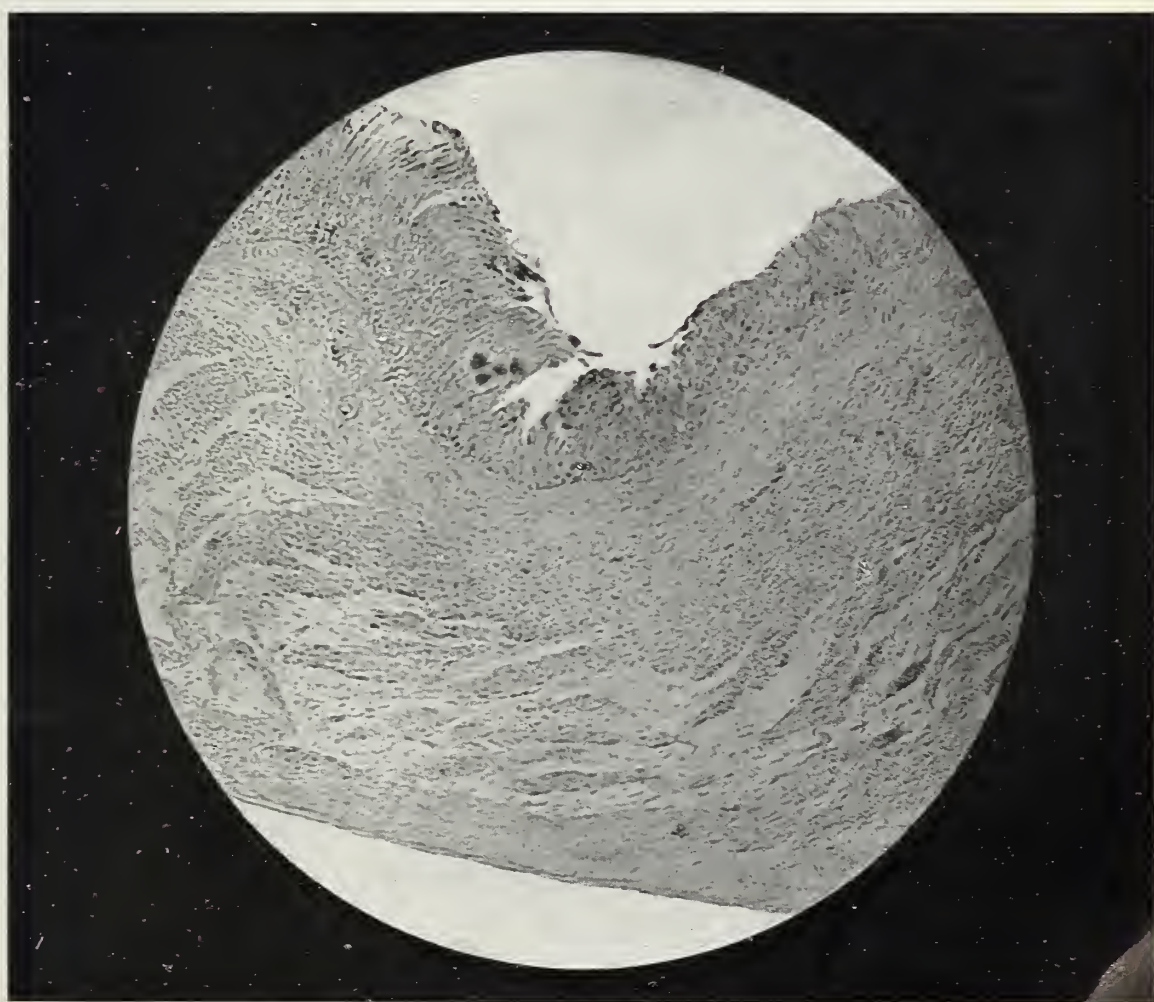


FIG. 8.—SAME AS 7. HIGHER MAGNIFICATION.

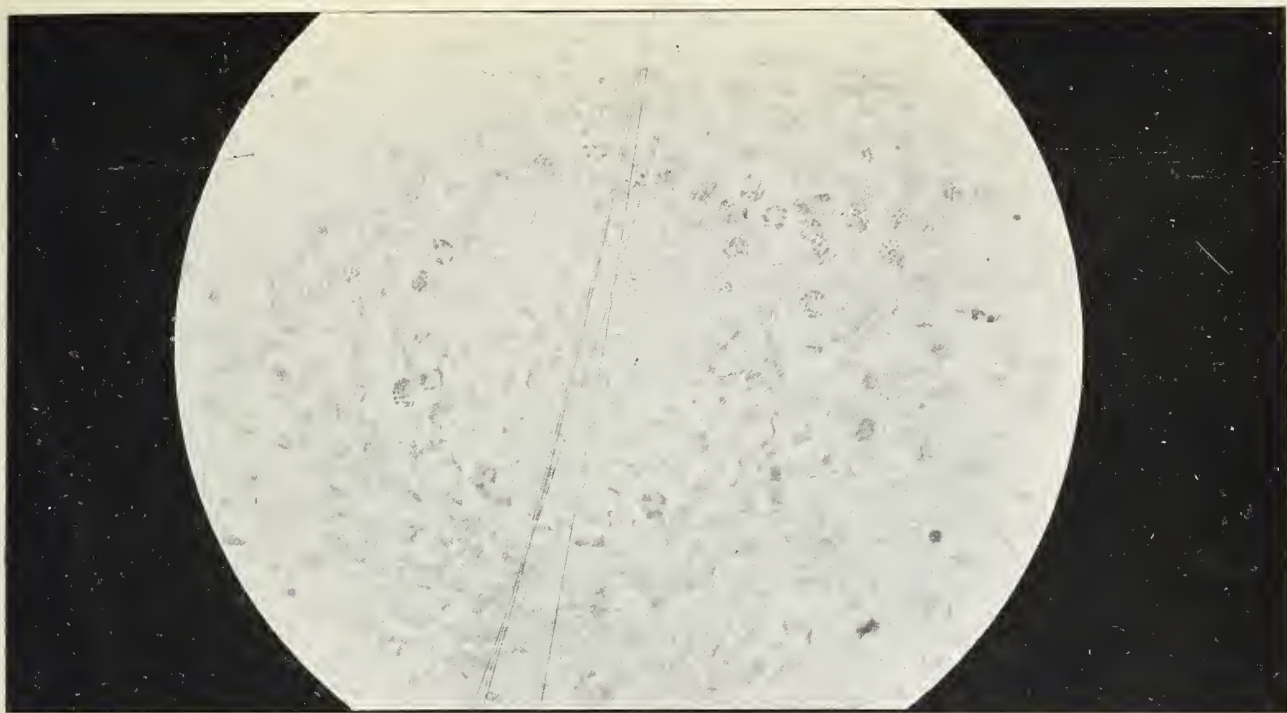


FIG. 9.—EOSINOPHILES GROUPED ABOUT PERIPHERY OF A SMALL BLOOD VESSEL.

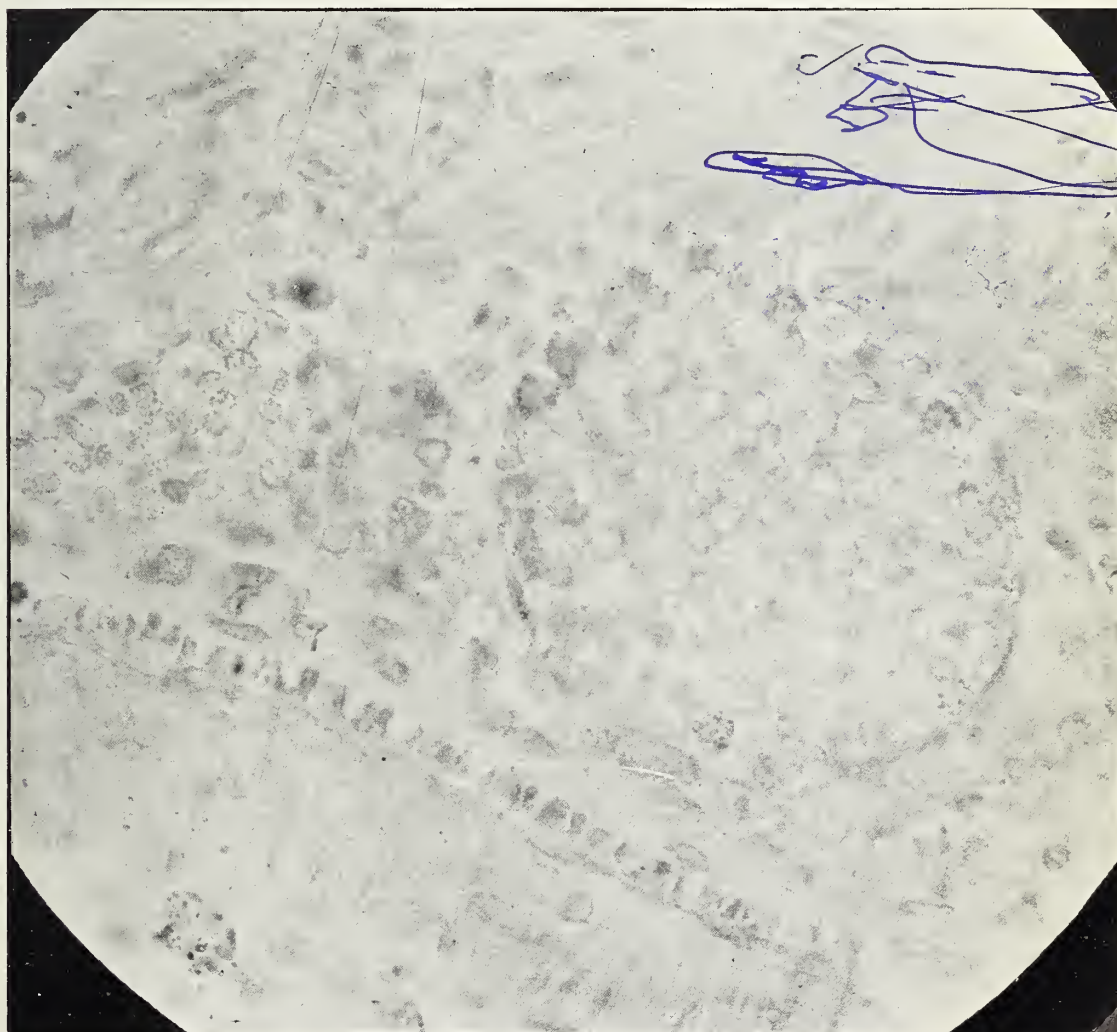


FIG. 10.—EOSINOPHILES GROUPED ABOUT PERIPHERY OF SMALL BLOOD VESSEL AT
BASE OF MUCOSA.



FIG. 11.—ULCER. NOTE ABSENCE OF CELLULAR INFILTRATION, INDICATING DIGESTION OF MUCOSA.

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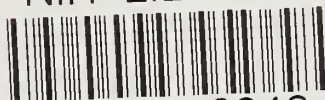


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